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SUPPLEMENT NUMBER 4 ON WAR MEDICINE AND SURGERY:

Traumatic Shock.

SOME FACTORS INFLUENCING BACTERIAL SURVIVAL IN THE PRESENCE OF ANTISEPTICS.

By J. J. GRAYDON and C. L. BIGGS.

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SPECIAL precautions are required when tests are made for viable organisms in the presence of mercurial antiseptics, owing to the ability of these compounds to inhibit bacterial growth in extremely high dilutions. Failure to observe these precautions and to distinguish between the killing of organisms and the inhibition of their growth has frequently resulted in the germicidal efficiency of these antiseptics being misrepresented.

Various methods may be employed to overcome the bacteriostasis due to substances of high inhibitory powers.

In order to ensure that the antiseptic carried over with the inoculum in disinfectant tests would be sufficiently diluted to prevent inhibition of growth, Shippen (1928) proposed that cultures should be made in large volumes of medium.

The degree of dilution necessary is greatly influenced by the fact that organisms once subjected to the action of antiseptic, though still viable, may be incapable of developing in a concentration of disinfectant which will freely permit the growth of organisms not previously exposed to antiseptics. This was illustrated by the following experiment:

A broth suspension containing 2,000,000,000 organisms per millilitre was prepared from a twenty-four hour agar culture of staphylococci (strain "Denis"). One millilitre of this suspension was added to eight millilitres of broth, to which one millilitre of a 1% solution of "Merthiolate" had been added. Five minutes later one millilitre of the mixture was

removed to make a series of dilutions in broth tubes. A second series of broth tubes containing the same concentrations of "Merthiolate" was seeded with inocula containing the same number of organisms as in the corresponding tubes of the first series. The results after incubation at 37° C. for seven days are given in Table I.

TABLE I.

Showing the Diminished Ability of Staphylococci Treated with a 1/1,000 Solution of "Merthiolate" for Five Minutes to Grow in Concentrations of "Merthiolate" which Fail to Inhibit Growth of Untreated Staphylococci.

Concentration of "Merthiolate" in Final Culture.	Calculated Number of Staphylococci in Final Culture.	Staphylococci Treated with "Merthiolate" (1/1,000) for Five Minutes.	Untreated Staphylococci.
1 in 1,000,000	20×10^4	—	—
1 in 4,000,000	5×10^4	—	+
1 in 20,000,000	1×10^4	—	+
1 in 200,000,000	0.1×10^4	+	+

— indicates no growth.

+ indicates growth.

Similar results have been obtained when staphylococci have been subjected for various times to the action of "Merthiolate" in concentrations of 1/5,000, 1/10,000 and 1/20,000 or to the action of "Merfenil" diluted to 1/20,000.

Further evidence of modification of bacteria by sublethal treatment with antiseptic is afforded by an increase in the time before growth of such organisms occurs on subculture in ordinary media. We have found that the lag period may extend to weeks or even months.

It is clear from these experiments that in the determination of the lowest dilution which will not inhibit growth, preliminary tests with untreated organisms give a misleading result. The use of volumes of medium sufficient

to dilute out completely the inhibitory action of mercurial antiseptics from adequate and representative samples may therefore prove impracticable.

As an alternative, Shippen suggested a procedure now commonly practised of making transfers from the first subcultures into fresh tubes of medium. Usually these transfers are made only from those tubes which have not shown growth—a procedure which is open to a serious objection. By the incubation of the subcultures in that way before the second transfers are made, the test organisms are subjected to the action of the antiseptic in low concentration at 37° C. With some disinfectants this may be sufficient to kill the organisms before the transfers are made.

In the experiment reported in Table II growth frequently resulted when transfers to the second tubes were made before the incubation of the original subcultures, whilst material transferred from the same tubes after twenty-four hours' incubation showed no growth.

A second objection to the successive transfer method is that the amount of the original sample taken over into the final tube of medium is inadequate if the distribution of viable organisms is scanty. Few, if any, bacteria may be included in the second transfer.

Garrod (1935) has shown that small inocula fail to grow in concentrations of antiseptic in which heavy inocula can freely multiply. The size of the inoculum, and the fact that one is usually dealing with "treated" organisms, must be borne in mind when the ultimate dilution of antiseptic required to eliminate bacteriostasis in both sterility and germicidal tests is being determined.

Garrod also found that small inocula containing few organisms failed to grow even when no recognized antiseptic was present in the medium. This phenomenon was studied in more detail by O'Meara and Macaween (1936, 1937), who attributed the inhibition of growth from small inocula to the presence of traces of copper in the medium. They found a definite relationship between the amount of copper present and the size of the inoculum required to produce growth.

In view of these findings, steps should be taken to see that all liquid media used in sterility or germicidal tests are "copper-free". O'Meara and Macaween describe the preparation of such a medium. We have found that the avoidance of copper utensils and the use of a peptone ("Difco" proteose) with negligible content of copper ensure a sufficiently low concentration of copper. McFarlane's diethyl dithiocarbamate method was used to estimate the amount of copper in our media; the highest value found was 0.13 milligramme per 100 millilitres, which appeared to be ineffective in preventing growth.

The possible use of surface growth on agar plates as a method of overcoming inhibition of growth by traces of mercurial antiseptics occurred to us during the course of investigations with staphylococcal toxins. It was observed that growth took place when these toxins containing 0.02% of "Merthiolate" were stroked upon the surface of agar plates, whereas similar samples inoculated into fluid media failed to grow. It was found, too, that a much greater

concentration of antiseptic was required to inhibit growth on the surface than was needed to prevent growth within the agar gel. Staphylococci, the growth of which was inhibited in fluid media by concentrations of "Merthiolate" less than 1/1,000,000, grew on the surface of nutrient agar containing ten times that amount of "Merthiolate".

By direct inoculation on the well-dried surface of nutrient agar we obtained growth of staphylococci treated with 1% "Merthiolate" solution for five minutes. Simultaneous inoculation into broth and into agar by the usual pour-plate method appeared to indicate the absence of viable organisms. The failure of the last procedure was probably due to the action of the antiseptic at the higher temperature of the melted agar. Estimations of germicidal efficiency from time-survivor curves based upon pour-plate colony counts may be open to criticism on this score.

When a heavily inoculated pour-plate was stroked with a 0.1% solution of "Merthiolate", a zone of inhibition of both surface and subsurface growth was apparent following incubation. When the inoculum was placed on the surface of the agar similar stroking with "Merthiolate" solution failed to produce any such zone. This indicated that in the pour-plates no organisms were actually on the surface of the agar. Colonies obtained on the surface of ordinary pour-plates are apparently the result of growth from near-surface organisms.

Disinfectant tests were performed, in which a loopful of each mixture of organisms and antiseptic was stroked directly upon the surface of agar plates and the results were compared with those obtained with the usual culture in broth and subsequent transfer method. Growth often appeared on the agar plate when it failed to appear in broth. However, technical difficulties were encountered which rendered the plate method too uncertain for adoption as a routine procedure for sterility tests. In certain circumstances it may be employed with advantage in disinfectant testing.

Of the various methods examined, it was found that the inclusion of thioglycolic acid or its sodium salt in the medium was the most satisfactory means of overcoming the bacteriostatic action of mercurial antiseptics. Media containing thioglycolic acid are also of great value because of their ability to promote growth of anaerobes without special apparatus (Quastel and Stephenson, 1926; O'Meara, 1937).

Cysteine has properties similar to those of thioglycolic acid when added to bacteriological media. For some time following the report of Hosoya (1927) we used cysteine in nutrient broth to maintain anaerobic cultures without taking any other precautions to produce anaerobiosis; but we found its rapid oxidation a decided disadvantage. Smith, Czarnetsky and Mudd (1936) noted that cysteine overcame the bacteriostatic action of mercurials.

The action of thioglycolic acid in the medium may be explained as follows. It is now generally accepted that the mercapto group (-SH) is necessary for the metabolism of most bacteria. This group may be present or potentially available in the medium, or it may be transferred in sufficient quantity with the inoculum.

TABLE II.
Showing Portion of a Disinfectant Test at 20° C. on "Merthiolate" with *Staphylococcus aureus* as the Test Organism;
Readings made after Forty-eight Hours' Incubation.

Concentration of "Merthiolate".	Five Minutes.			Ten Minutes.			Fifteen Minutes.		
	First Subculture.	Immediate Retransfer.	Retransfer after Incubation for 24 Hours.	First Subculture.	Immediate Retransfer.	Retransfer after Incubation for 24 Hours.	First Subculture.	Immediate Retransfer.	Retransfer after Incubation for 24 Hours.
1/100	+	+	+	+	+	+	+	+	+
1/200	+	+	+	+	+	+	+	+	+
1/400	+	+	+	+	+	+	+	+	+
1/800	+	+	+	+	+	+	+	+	+
1/2,000	+	+	+	+	+	+	+	+	+
1/4,000	+	+	+	+	+	+	+	+	+
1/8,000	+	+	+	+	+	+	+	+	+
1/16,000	+	+	+	+	+	+	+	+	+
1/32,000	+	+	+	+	+	+	+	+	+
1/64,000	+	+	+	+	+	+	+	+	+
1/128,000	+	+	+	+	+	+	+	+	+
1/256,000	+	+	+	+	+	+	+	+	+
1/512,000	+	+	+	+	+	+	+	+	+
1/1,024,000	+	+	+	+	+	+	+	+	+
1/2,048,000	+	+	+	+	+	+	+	+	+
1/4,096,000	+	+	+	+	+	+	+	+	+
1/8,192,000	+	+	+	+	+	+	+	+	+
1/16,384,000	+	+	+	+	+	+	+	+	+
1/32,768,000	+	+	+	+	+	+	+	+	+
1/65,536,000	+	+	+	+	+	+	+	+	+
1/131,072,000	+	+	+	+	+	+	+	+	+
1/262,144,000	+	+	+	+	+	+	+	+	+
1/524,288,000	+	+	+	+	+	+	+	+	+
1/1,048,576,000	+	+	+	+	+	+	+	+	+
1/2,097,152,000	+	+	+	+	+	+	+	+	+
1/4,194,304,000	+	+	+	+	+	+	+	+	+
1/8,388,608,000	+	+	+	+	+	+	+	+	+
1/16,777,216,000	+	+	+	+	+	+	+	+	+
1/33,554,432,000	+	+	+	+	+	+	+	+	+
1/67,108,864,000	+	+	+	+	+	+	+	+	+
1/134,217,728,000	+	+	+	+	+	+	+	+	+
1/268,435,456,000	+	+	+	+	+	+	+	+	+
1/536,870,912,000	+	+	+	+	+	+	+	+	+
1/1,073,741,824,000	+	+	+	+	+	+	+	+	+
1/2,147,483,648,000	+	+	+	+	+	+	+	+	+
1/4,294,967,296,000	+	+	+	+	+	+	+	+	+
1/8,589,934,592,000	+	+	+	+	+	+	+	+	+
1/17,179,869,184,000	+	+	+	+	+	+	+	+	+
1/34,359,738,368,000	+	+	+	+	+	+	+	+	+
1/68,719,476,736,000	+	+	+	+	+	+	+	+	+
1/137,438,953,472,000	+	+	+	+	+	+	+	+	+
1/274,877,906,944,000	+	+	+	+	+	+	+	+	+
1/549,755,813,888,000	+	+	+	+	+	+	+	+	+
1/1,099,511,627,776,000	+	+	+	+	+	+	+	+	+
1/2,199,023,255,552,000	+	+	+	+	+	+	+	+	+
1/4,398,046,511,104,000	+	+	+	+	+	+	+	+	+
1/8,796,093,022,208,000	+	+	+	+	+	+	+	+	+
1/17,592,186,044,416,000	+	+	+	+	+	+	+	+	+
1/35,184,372,088,832,000	+	+	+	+	+	+	+	+	+
1/70,368,744,177,664,000	+	+	+	+	+	+	+	+	+
1/140,737,488,355,328,000	+	+	+	+	+	+	+	+	+
1/281,474,976,710,656,000	+	+	+	+	+	+	+	+	+
1/562,949,953,421,312,000	+	+	+	+	+	+	+	+	+
1/1,125,899,906,842,624,000	+	+	+	+	+	+	+	+	+
1/2,251,799,813,685,248,000	+	+	+	+	+	+	+	+	+
1/4,503,599,627,370,496,000	+	+	+	+	+	+	+	+	+
1/9,007,199,254,740,992,000	+	+	+	+	+	+	+	+	+
1/18,014,398,509,481,984,000	+	+	+	+	+	+	+	+	+
1/36,028,797,018,963,968,000	+	+	+	+	+	+	+	+	+
1/72,057,594,037,927,936,000	+	+	+	+	+	+	+	+	+
1/144,115,188,075,855,872,000	+	+	+	+	+	+	+	+	+
1/288,230,376,151,711,744,000	+	+	+	+	+	+	+	+	+
1/576,460,752,303,423,488,000	+	+	+	+	+	+	+	+	+
1/1,152,921,504,606,846,976,000	+	+	+	+	+	+	+	+	+
1/2,305,843,009,213,693,952,000	+	+	+	+	+	+	+	+	+
1/4,611,686,018,427,387,904,000	+	+	+	+	+	+	+	+	+
1/9,223,372,036,854,775,808,000	+	+	+	+	+	+	+	+	+
1/18,446,744,073,709,551,616,000	+	+	+	+	+	+	+	+	+
1/36,893,488,147,419,103,232,000	+	+	+	+	+	+	+	+	+
1/73,786,976,294,838,206,464,000	+	+	+	+	+	+	+	+	+
1/147,573,952,589,676,412,928,000	+	+	+	+	+	+	+	+	+
1/295,147,905,179,352,825,856,000	+	+	+	+	+	+	+	+	+
1/590,295,810,358,705,651,712,000	+	+	+	+	+	+	+	+	+
1/1,180,591,620,717,411,303,424,000	+	+	+	+	+	+	+	+	+
1/2,361,183,241,434,822,606,848,000	+	+	+	+	+	+	+	+	+
1/4,722,366,482,869,645,213,696,000	+	+	+	+	+	+	+	+	+
1/9,444,732,965,739,290,427,392,000	+	+	+	+	+	+	+	+	+
1/18,889,465,931,478,580,854,784,000	+	+	+	+	+	+	+	+	+
1/37,778,931,862,957,161,709,568,000	+	+	+	+	+	+	+	+	+
1/75,557,863,725,914,323,419,136,000	+	+	+	+	+	+	+	+	+
1/151,115,727,451,828,646,838,272,000	+	+	+	+	+	+	+	+	+
1/302,231,454,903,657,293,677,544,000	+	+	+	+	+	+	+	+	+
1/604,462,909,807,314,587,355,088,000	+	+	+	+	+	+	+	+	+
1/1,208,925,819,614,629,174,710,176,000	+	+	+	+	+	+	+	+	+
1/2,417,851,639,229,258,349,420,352,000	+	+	+	+	+	+	+	+	+
1/4,835,703,278,458,516,698,840,704,000	+	+	+	+	+	+	+	+	+
1/9,671,406,556,917,033,397,681,408,000	+	+	+	+	+	+	+	+	+
1/19,342,813,113,834,066,795,362,816,000	+	+	+	+	+	+	+	+	+
1/38,685,626,227,668,133,590,725,632,000	+	+	+	+	+	+	+	+	+
1/77,371,252,455,336,267,181,451,264,000	+	+	+	+	+	+	+	+	+
1/154,742,504,910,672,534,362,902,528,000	+	+	+	+	+	+	+	+	+
1/309,485,009,821,345,068,725,805,056,000	+	+	+	+	+	+	+	+	+
1/618,970,019,642,690,137,451,610,112,000	+	+	+	+	+	+	+	+	+
1/1,237,940,039,285,380,274,903,220,224,000	+	+	+	+	+	+	+	+	+
1/2,475,880,078,570,760,549,806,440,448,000	+	+	+	+	+	+	+	+	+
1/4,951,760,157,141,521,099,612,880,896,000	+	+	+	+	+	+	+	+	+
1/9,903,520,314,283,042,199,225,771,779,392,000	+	+	+	+	+	+	+	+	+
1/19,807,040,628,566,084,398,451,543,558,784,000	+	+	+	+	+	+	+	+	+
1/39,614,081,257,132,168,796,903,087,117,568,000	+	+	+	+	+	+	+	+	+
1/79,228,162,514,264,337,593,806,174,235,136,000	+	+	+	+	+	+	+	+	+
1/158,456,325,028,528,675,187,612,348,470,272,000	+	+	+	+	+	+	+	+	+
1/316,912,650,057,057,350,375,224,696,940,544,000	+	+	+	+	+	+	+	+	+
1/633,825,300,114,114,700,750,450,449,081,088,000	+	+	+	+	+	+	+	+	+
1/1,267,650,600,228,229,401,500,900,898,162,176,000	+	+	+	+	+	+	+	+	+
1/2,535,301,200,456,458,803,001,801,796,324,352,000	+	+	+	+	+	+	+	+	+
1/5,070,602,400,912,917,606,002,403,582,648,704,000	+	+	+	+	+	+	+	+	+
1/10,141,204,801,825,835,212,004,805,165,297,408,000	+	+	+	+	+	+	+	+	+
1/20,282,409,603,651,670,424,008,010,325,584,816,000	+	+	+	+	+	+	+	+	+
1/40,564,819,207,303,340,848,016,020,651,169,632,000	+	+	+	+	+	+	+	+	+
1/81,129,638,414,606,681,696,032,041,302,339,264,000	+	+	+	+	+	+	+	+	+
1/162,259,276,829,213,363,392,064,082,604,678,528,000	+	+	+	+	+	+	+	+	+
1/324,518,553,658,426,726,784,128,165,209,357,056,000	+	+	+	+	+	+	+	+	+
1/649,037,107,316,853,453,568,256,330,418,714,112,000	+	+	+	+	+	+	+	+	+
1/1,298,074,214,633,706,907,136,512,660,837,428,224,000	+	+	+	+	+	+	+	+	+
1/2,596,148,429,267,413,814,273,025,321,674,856,448,000	+	+	+	+	+	+	+	+	+
1/5,192,296,858,534,827,628,546,050,643,349,712,896,000	+	+	+	+	+	+	+	+	+
1/10,384,593,717,069,655,257,109,210,128,689,425,792,000	+	+	+	+	+	+	+	+	+
1/20,769,187,434,139,310,514,218,420,257,378,851,584,000	+								

Compounds of mercury unite with the mercapto groups to form a compound devoid of the -SH grouping, thereby depriving the bacterial cell of an essential metabolite and preventing growth. This reaction is reversed within limits by the addition of compounds of the type R-SH, of which thioglycolic acid is one (Fildes, 1940). In this way mercapto compounds may be said to neutralize specifically the antibacterial action of mercurials. They may also rectify any deficiency of mercapto groupings in the medium, thereby permitting growth from small inocula.

When sufficient thioglycolic acid is added to the medium, the resultant lowering of the oxidation potential enables anaerobic bacteria to grow with a considerably diminished latent period. The presence of glucose in thioglycolic acid media is advantageous, because it provides by hydrolytic cleavage a ready source of energy to promote growth of strict aerobes.

The action of copper may be thus explained. Traces of copper catalyse the oxidation of -SH groupings, both within the cell and in the medium (O'Meara, 1937). When few of these groups are present, as is the case when a small inoculum is transferred to a medium devoid of mercapto groupings, this action of copper may prevent growth. The addition of substances containing the mercapto group to the medium temporarily offsets the effect of copper; but the latter, by its catalytic oxidizing action on the added compound, will eventually reduce it to impotence. Thus thioglycolic acid cannot be expected to maintain its activity for a long period in a medium that is not copper-free.

In nutrient broth containing a 0.05% concentration of thioglycolic acid most anaerobes will grow. However, Hitchen's medium to which this acid has been added provides a most valuable medium for general purposes for performance of both sterility and germicidal tests, particularly in the presence of mercurial antiseptics (Morgan, Simmons and Biggs, 1942).

Summary.

1. Methods are discussed for overcoming the inhibitory action of antiseptics in germicidal and sterility tests.
2. The influence of previous exposure to antiseptics on the subsequent growth of bacteria is stressed.
3. The importance of using copper-free media is emphasized.
4. The use of thioglycolic acid or sodium thioglycollate in media is recommended for tests of bacterial survival.

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POOLED HUMAN SERUM: A NOTE ON TESTING FOR STERILITY IN THE PRESENCE OF CERTAIN ANTISEPTICS.

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Owing to the widespread use of pooled human serum or plasma for continuous transfusion, many laboratories have been concerned in its production, both here and abroad, during this war. In its preparation one must make, as a matter of routine, tests for sterility to ensure freedom from bacterial contamination before distribution. Regulations which govern the routine performance of such tests exist in many countries; they have been in force for many years, notably in Great Britain and in the United States of America. Tests customarily made at the Commonwealth Serum Laboratories include those prescribed in Great Britain and extra tests also regarded as valuable.

Regulations usually prescribe the maximum amount of antiseptic which is permissible after dilution with the medium, so that no inhibition of growth of viable organisms may occur.

The perfect antiseptic for use in biological products has not been discovered. For many years phenolic preservatives have been extensively employed by manufacturers; but these valuable antiseptics possess two notable disadvantages, in that they tend to precipitate serum protein and are incompatible with products containing formaldehyde.

Sodium ethyl mercurithiosalicylate—"Merthiolate" (Eli Lilly and Company)—does not possess these particular disadvantages to an appreciable degree and has been used for special purposes in consequence. Whereas phenolic preservatives are bacteriostatic only in relatively high concentrations (more than 0.01%), "Merthiolate" is bacteriostatic in great dilutions. Under certain conditions it has been found to inhibit growth of bacteria when diluted to one part in forty millions. This fact has, in the past, constituted a handicap, because the usually generous sampling of a product was not possible. The cost and volume of media required for each test made its use impracticable.

This problem has been most satisfactorily solved by the use of sterility test media containing either sodium thioglycollate or thioglycolic acid. Prior to this, however, experimental work here had shown that Hitchen's medium alone was a satisfactory test medium, provided the concentration of antiseptic was within certain limits; to this point reference will be made later.

For many years it has been our custom to employ "Merthiolate" and another mercurial antiseptic—"Merfenil" (May and Baker)—in veterinary vaccines and in certain bacteriological diagnostic agents. Many million doses of these vaccines, which contain small amounts of formaldehyde, have been given to stock without apparent harmful effect. Test doses as large as 50 millilitres have been given intramuscularly to sheep, with no ill effect other than at times a transient lameness.

As it was necessary to add an antiseptic to pooled human serum for continuous transfusion, it was decided to use "Merthiolate" in a dilution of 1 part in 10,000. In 1939 and 1940 such serum in doses of 600 millilitres or 1,000 millilitres was given intravenously to patients in hospital, with no ill effects.

We were also encouraged by much earlier reports of the use of "Merthiolate" in the United States of America as a preservative in biological products for human use. Nevertheless, the dosage was small compared with that proposed for intravenous transfusion of serum.

At the time doubts were expressed concerning the possible toxicity of the antiseptic that might follow administration of large volumes of serum. Subsequent experience has shown that two litres of serum caused no perceptible toxic effects among a large number of casualties treated with serum given intravenously. Doses of serum

up to 10 litres have been reported (verbal communication) to have been associated with no apparent harmful effects.

Various workers have reported on the use of media containing either thioglycolic acid or sodium thioglycolate, and have found with these additions that the growth of anaerobes is possible under "aerobic" conditions and that bacteria grow in the presence of relatively large amounts of mercurial antiseptics.

O'Meara (1937) made observations on the type of chemical adjustments required to enable a strict anaerobe, such as *Clostridium tetani*, to grow from very small inocula in fluid media freely exposed to atmospheric oxygen. He used in his experiments a nutrient broth of pH 7.3, to which he added thioglycolic acid to give a final concentration of 0.05%. Comparative results of tests made with *Clostridium tetani* in an anaerobic jar and of tests made in broth, plus thioglycolic acid, indicated that the two methods of cultivation were about equally efficient.

Brewer (1940) employed a clear pork infusion medium containing 0.05% agar, 0.1% sodium thioglycolate and 1% dextrose. He found this medium to be satisfactory for the growth of strict anaerobes, without any special precautions to provide further anaerobic conditions (for example, an anaerobic jar), even if the medium had been stored for one month at room temperature prior to inoculation. He found, too, that sodium thioglycolate combined with and inactivated most of the mercurials used as preservatives, and suggested the use of this medium for testing the sterility of biological preparations, of catgut sutures and similar material. He obtained the same results with a medium containing thioglycolic acid; but the pH of the medium had to be readjusted.

Marshall, Gunnison and Luxen (1940) used Brewer's medium in testing biological products for sterility. Their results support Brewer's claims that thioglycolate, added to the medium, permits the growth of viable organisms in the presence of "Merthiolate" and that cultivation of anaerobes is facilitated.

Reid and Bowditch (1942) used Brewer's medium in conjunction with infusion broth and blood agar plates. They cultivated 69 samples of blood and 93 uterine specimens in this medium and obtained results which favoured the thioglycolate medium. They recommend its use for routine diagnostic bacteriology.

Experimental Work.

The trial of media containing 0.1% thioglycolic acid for sterility tests was commenced at these laboratories two years ago. Our results confirm in general the claims of Brewer, and those of Marshall and others.

For many years a modified Hitchen's medium has been used by us for routine testing of the sterility of products, and it is an excellent medium for the growth of both aerobic and anaerobic organisms. Our modification of Hitchen's medium yields a clear, semi-solid medium of pH 7.2. Our method of preparation is described below, and also that of a modified Hitchen's medium of higher pH for the addition of thioglycolic acid.

Method of Preparation of Hitchen's Medium (Modified).

Hitchen's medium is prepared as follows:

To 500 grammes of minced veal, free from fat, add one litre of distilled water, and the mixture is stored at 4° C. overnight. Boil for twenty minutes, press, cool and siphon

off. Titrate to pH 7.0, add 1% proteose peptone ("Difco") and 0.5% sodium chloride, and boil for five minutes. Titrate to pH 8.0 (8.8),¹ boil for five minutes, and filter through paper. Add 0.1% of abraded agar and autoclave at 15 pounds' pressure for fifteen minutes. Add 0.1% glucose and filter through paper. Readjust pH to 8.0 (8.8). Bottle in quantities of 150 millilitres and autoclave at 12.5 pounds' pressure for thirty minutes. The medium should be crystal clear and free from precipitate.

Method of Preparation of Thioglycolic Acid (10% Solution).

Thioglycolic acid solution may be made up in sterile distilled water (preferably all glass-distilled) and placed in a number of small, sterile, air-tight containers. These are freshly sterilized by being completely immersed in cold water, which is then brought to the boil and kept boiling for ten minutes (O'Meara, 1937). Only sufficient of a 10% solution to last for one to three weeks is prepared, and from this solution are pipetted, with aseptic precautions, 1.5 millilitres to each 150 millilitres of Hitchen's medium. The pH of the special Hitchen's medium drops from approximately 8.1 to approximately 7.1 on the addition of the thioglycolic acid. The bottles containing thioglycolic acid are prepared daily according to the number required for the day's tests. As a routine measure, Hitchen's medium is steamed for one hour and cooled just prior to inoculation. The special Hitchen's medium is also steamed prior to the addition of the thioglycolic acid; this steaming is regarded as preferable, but not absolutely essential.

Brewer's medium closely resembles Hitchen's medium. Significantly, both contain a small percentage of agar. The presence of agar in the medium is regarded by us as important. The precise way in which it functions is obscure and is the subject of controversy. The details of preparation of Brewer's medium have not been stated in his paper, but the constituents of the medium have been given.

Discussion.

For the detection of viable organisms we regard Hitchen's medium as superior to infusion broth. Moreover, without the addition of thioglycolic acid it has the effect of reducing the inhibitory action of "Merthiolate". Our experience has been that, in this medium alone, added staphylococci show obvious growth within twenty-four hours in a concentration of "Merthiolate" varying from 1/100,000 to 1/1,500,000. In our routine tests in the dilution of our samples we have always arranged that the amount of this antiseptic should be within these limits. When infusion broth is used with these amounts of antiseptic, there is no growth of the added staphylococci, even after seven days' incubation at 37° C. When staphylococci are added to broth and Hitchen's medium containing 0.1% thioglycolic acid, growth is obtained in twenty-four hours, even in a concentration of "Merthiolate" of 1/1,000.

Since the beginning of this war we have added to the pooled human serum, in the wet form, sufficient "Merthiolate" to give a theoretical concentration of one

¹ Figures in parentheses refer to the pH required when special Hitchen's medium is being prepared for the addition of a 10% solution of thioglycolic acid.

TABLE I.
Growth of Staphylococci in Media Containing "Merthiolate", with and without the Addition of 0.1% Thioglycolic Acid.

Medium.	Concentration of "Merthiolate".	Organism Added.	Result of Incubation at 37° C.	
			0.1% Thioglycolic Acid Added.	Without Thioglycolic Acid.
Hitchen's medium	1/1,000-1/50,000	Staphylococcus.	+1 ²	-7 ²
Hitchen's medium	1/100,000-1/1,500,000	Staphylococcus.	+1	+1
Glucose broth	1/1,000-1/50,000	Staphylococcus.	+1	-7
Glucose broth	1/100,000-1/1,500,000	Staphylococcus.	+1	-7

+ = growth of staphylococci. - = no growth visible.

² Figure = number of days.

TABLE II.
Routine and Additional Sterility Tests Performed on Pooled Human Serum
Containing "Merthiolate".

Medium Used.	Volume of Medium.	Amount of Inoculum. (Millilitres.)	Temperature During Incubation for Seven Days.
0.1% glucose infusion broth.	100 ml. in 200 ml. Florence flask.	2.0	37° C.
0.1% glucose infusion broth.	100 ml. in 200 ml. Florence flask.	2.0	Room temperature.
Meat medium.	15 ml. in 6 in. x 1 in. test tube.	0.25	37° C.
Hitchen's medium.	150 ml. in 200 ml. bottle.	3.0	37° C.
Hitchen's medium containing 0.1% thioglycolic acid.	150 ml. in 200 ml. bottle.	3.0	37° C.

part in ten thousand. The volume of the sample for test, when added to the bottle of the test medium, yields a final concentration of "Merthiolate" of one part in half a million.

It should be noted here that, whereas "Merthiolate" in dilutions of 1/100,000 to 1/1,500,000 may not inhibit the growth of a large inoculum of staphylococci in Hitchen's medium, without thioglycolic acid, nevertheless these amounts of antiseptic may still be inhibitory for other organisms, which have already been subjected to the action of a concentration of "Merthiolate" of 1/10,000 in the product during storage. In such cases when 0.1% thioglycolic acid is added to the culture medium, the organisms thus damaged prove viable after incubation overnight. Organisms exposed to a concentration of 1/1,000 of "Merthiolate" for seven days at 5° C. have been proved viable by the use of the thioglycolic medium under these conditions.

In the performance of tests for sterility, it has been our custom to take two samples of serum for the test, each of 15 millilitres, one at the beginning of bottling and one at the end, from a batch of 20 litres of pooled human serum. Thus, if viable organisms are present, they should be detectable by an adequate technique, even if only one organism is present in some 30 millilitres of serum.

For many years we have incubated test material, both at room temperature and at 37° C. The lower temperature is valuable, as it favours the development of moulds, if they are present as contaminants. The extra sample for the room temperature test is taken only at the end of bottling. All material undergoing tests for sterility is examined daily for seven days; then, if there is no evidence of bacterial growth to the naked eye, or when a hand lens is used, the material is pronounced sterile.

The tests described in this note refer only to tests to detect any contaminating organisms after bottling (final sterility test). Other tests include those made as a routine measure for viable organisms of any kind prior to bottling and those upon bulk batches or products during the course of preparation.

A much larger inoculum than the three millilitres used by us can be added to each bottle of thioglycolic medium with perfect safety, if it is so desired.

By means of the modified medium described herein, the proportion of serum to medium has been experimentally increased ten to twenty times without clouding of the mixture.

An initial difficulty in the introduction of the use of thioglycolic acid as a routine measure was encountered in the early stages of this work, for it was available to us only in very small quantity, barely enough for experiment. We eventually obtained a quantity from British Drug Houses Limited, London, and an additional quantity was prepared locally for us by Alfred Lawrence and Company, of Melbourne. Both samples proved equally satisfactory in our experience.

Many comparative tests were performed with a number of different bacteria, aerobic and anaerobic. All showed the value of thioglycolic acid as an aid to bacterial growth.

In this issue Graydon and Biggs (1942) discuss the theory underlying the mechanism of the action of thioglycolic acid in culture media.

Summary.

1. The tests and the media used at the Commonwealth Serum Laboratories for testing sterility of pooled human serum in the presence of "Merthiolate" are briefly indicated.

2. The use of thioglycolic medium is strongly recommended as a medium for sterility testing, and the claims of other workers are supported.

3. Attention is drawn to the suitability of thioglycolic or thioglycollate medium for routine diagnostic work, particularly for the cultivation of anaerobes and especially in the absence of other facilities for obtaining anaerobiosis.

4. A method is described for the preparation of modified Hitchen's medium, to which thioglycolic acid can be added.

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FURTHER NOTES ON THE CONTROL OF POST-PARTUM HÆMORRHAGE BY INJECTION OF THE UMBILICAL VEIN.

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In an article on difficulties in the third stage of labour published in 1939,⁽¹⁾ I gave a brief account of the origin and history of the method of treating the retained placenta by injection of the umbilical vein. This history was quoted from an article by Jarcho,⁽²⁾ describing three cases in which he had successfully employed the method. I would recommend anyone interested in the history of this procedure to look up his summary, which was condensed from a complete history published in 1925 by W. Koerting. After Mojon first described this procedure in 1826, it was during the next hundred years occasionally tried with some successes and apparently many failures, owing to faulty technique and lack of asepsis, until in 1914 Gabaston, of Buenos Aires, described a new and improved method. In 1937, Currie⁽³⁾ suggested the use of a Higginson instead of a "Record" syringe. With this there is no refilling to be done and the injection can be made more rapidly—a point which undoubtedly increases the efficiency of the operation.

In my previous article, I gave details of 18 cases in which the method had been used and found of great value, not only in assisting the separation and expulsion of the retained placenta, but also in providing a safe method of giving a hot intrauterine douche and controlling hæmorrhage in the third stage of labour. Since then, I have used this procedure in 51 further cases for varying reasons. I am more than ever convinced that a method of preventing and controlling post-partum hæmorrhage and of avoiding the dangerous operation of manual removal of the placenta, which is so simple and safe if carried out with proper precautions, should be more widely known and practised by the medical profession. I feel impelled to draw attention again to this simple operation, because none of the resident

medical officers joining our hospitals after graduation know anything of its use beyond seeing brief references to it in text-books. Apparently it is not taught in the practical midwifery work, and they are not told that the procedure has any value or encouraged to learn the technique. Lecturers and demonstrators seem satisfied to teach them how to perform manual removals in those cases in which Cr  d   expression has failed, and the patient has become exsanguinated and is suffering from shock. Earlier in the year, while going through the wards of one of the largest mainland hospitals, I saw a patient seriously ill with septic  mia following a manual removal. The resident medical officer, when asked if a cord injection had first been tried, said: "No, it hasn't, and what is it, anyway?" He had never heard of the procedure. In my opinion, any medical practitioner who proceeds to perform a manual removal without first trying a cord injection is (to put it mildly) not acting in the best interests of the patient. Students are rightly taught the importance of preventing undue blood loss, and it seems to me a pity that emphasis is not placed on the importance of trying this cord injection technique before adopting more serious operations, before causing shock to the patient with repeated attempts at Cr  d   expression, and before the patient has lost an abnormal amount of blood.

It is our duty to alleviate labour pain as far as possible. In striving for the ideal of painless labour, we may push narcotics to such a degree that too many babies are born suffering from asphyxia, and third stage complications become unduly frequent. Apart from the effects on the baby, there is no doubt that the administration of analgesics and anaesthetics during labour does predispose the patient to increased loss of blood and to a prolonged third stage. De Lee is of the opinion that we have gone too far in our efforts to relieve the pain of labour. This may be so; but even when they are used in moderation, such drugs will in some cases produce untoward effects on mother or child.

Currie¹⁰ has stressed the value of cord injection as a prophylactic measure against post-partum haemorrhage, and in the great majority of cases in the present series it was used for this purpose. In a few, in which there had been special difficulties of interference in the second stage, it was carried out immediately after the baby was separated, in anticipation of trouble from an exhausted uterus. In all cases of "atonic uterus", in which there is a tendency to steady haemorrhage, even though the amount of blood lost may not be immediately alarming, it is my practice to inject the cord before the patient shows signs of distress, if massaging of the fundus does not check the oozing. As a general rule, it is considered that a blood loss of over 20 ounces is an indication for injection, unless the placenta is obviously separated and can be delivered readily by Cr  d   expression.

Equipment.

The simple equipment should always be at hand in the labour ward, sterilized, or ready to be sterilized, so that there need be no delay if a sudden haemorrhage occurs. I always carry a small outfit in my bag or motor car. I have two "Sterilendum" enema syringes; one is fitted with a small bone enema nozzle filed as thin as possible and roughened on the surface to make a hold for the ligature; the other has a large-bore needle, round which I have soldered two or three small lead rings, which hold the ligature and make the needle less likely to move and transfix the vein. The needle is used when vessels in the cord are small, but I prefer the bone nozzle. If the syringe and sterile normal saline solution are always ready in the labour ward, it will be found that they will be used more and more frequently by doctors, who will learn to appreciate their value in cases of haemorrhage in the third stage of labour. Though perhaps it is not essential, I always carry a wire gauze cover with a small central hole, through which the end of the syringe passes into the jug of saline solution. It has a rim which fits over an ordinary two-pint jug, and it is, of course, sterilized. This keeps the bulb from falling into the saline solution after the syringe has been filled and while the nozzle is being

inserted into the cord vein. It is an extra precaution to prevent possible contamination of the saline solution by the bulb, which has been handled.

Technique.

The following is a brief description of this simple procedure.

1. When the baby is being separated, two ligatures or a ligature and a clamp are always applied and the cord is cut between them. This prevents the cord from emptying itself; the vessels remain distended, and are easy to inject.

2. It is important that the saline solution should be at such a temperature that when it reaches the uterus, it will be from 47   C. (115   F.) to 49   C. (120   F.). This will depend on the length of the cord or the distance from the point of injection in the cord to the uterus. The temperature drops about 5   C. (10   F.) if the distance is 12 to 15 inches, and I always begin injecting with the saline solution at a temperature varying from 52.5   C. (125   F.) to 54   C. (130   F.). I stress this point, because the saline solution used by Currie, Jarcho and others was at body temperature when injected, and would therefore be much below blood heat after it had traversed the cord and reached the placenta. I have repeatedly demonstrated that the uterus responds to saline solution at the higher temperature more quickly and powerfully than is the case with saline solution at body temperature.

3. The dependent part of the cord is sterilized by immersion in a bowl of spirit, while preparations are being made. The syringe is filled, and to prevent the entry of air, a forceps is clamped near the nozzle while the vein is being nicked and the nozzle introduced and tied in place. A forceps clamped on the cord just below the site to be injected is convenient as a holder.

4. The saline solution is now pumped in as rapidly as possible, and the result is often dramatic. The uterus, which has been slack, quickly contracts, and haemorrhage ceases. The placenta may be spontaneously expelled, or it can be expressed at once or in a few minutes by Cr  d  's manoeuvre. The amount of saline solution used is from one pint (568 cubic centimetres) to two pints (1,136 cubic centimetres) and I always have two pints ready in the jug.

In those cases in which retention of the placenta is caused by an hour-glass or localized contraction, the response is, of course, not the same. The placenta becomes separated and the uterus contracts; but this does not release the imprisoned part of the placenta. If haemorrhage has occurred, this usually ceases. Anaesthesia will often relax the spasm if it persists, and when preparation has been made for a manual removal, one can usually withdraw the firm, engorged placenta easily, with nothing but the hand in the vagina.

Analysis of 51 Cases.

In this series the proportion of cases in which injection was used was about one in twelve. This figure is probably higher than would be found necessary in general practice, because a certain number of the patients had abnormalities and were sent to me from the country, and in other cases I used the method to investigate its value. The results may be tabulated as follows:

Spontaneous delivery during injection	6 (11.8%)
Placenta expressed immediately after injection	24 (47.1%)
Placenta expressed within five minutes of injection	15 (29.4%)
Partial failures	4 (7.8%)
Failures	2 (3.9%)

Partial failures were those in which the placenta could not be expressed, but was removed with the hand in the vagina only. All four of these patients had contractions nipping and holding a part of the engorged placenta. All the placenta were easily pulled out complete by the hand in the vagina and without intrauterine interference.

One of the failures occurred in a case of preeclamptic tox  mia associated with an irregularly contracted uterus. The injection failed, and after three hours a manual removal was performed and two-thirds of the placenta were found to

be free in the uterus below a high contraction ring at the fundus. A small part was densely adherent and without any apparent cleavage line; it was scraped off with difficulty and with uncertainty as to its complete removal. I considered it to be a partial placenta accreta. The patient developed pyrexia, which, however, subsided under sulphanilamide therapy.

The second failure was in a case of poliomyelitis; but this condition was not blamed for the difficulties encountered. The patient was pregnant for the third time and had quick first and second stages; but the third stage lasted for three hours. A definite hour-glass contraction in the centre of the body of the uterus was palpable all through the third stage, and as the patient was not losing much blood, I did not hurry its completion. At one hour I gave 1.0 cubic centimetre of pituitrin without result. At two hours I injected the cord twice without success. At three hours a manual removal was performed. The placenta was engorged and completely separated, and the ring was tight and difficult to dilate; but when it was dilated, the placenta was easily extracted complete. It is likely that the pituitrin did harm in preventing relaxation of the ring.

Morbidity During the Puerperium.

In 43 cases there was no morbidity during the puerperium. Eight patients had a mild rise of temperature up to 100° F. lasting from a few days to a week; in all these cases some interference had been necessary—there were no normal deliveries among them. In two there was an impacted frank breech presentation, the patients being *primiparae*. In five forceps delivery was required, including a manual rotation for a persistent occipito-posterior position and a "high forceps" delivery.

In another forceps delivery failed; the patient was an elderly *primipara*, and I eventually performed a craniotomy. This was an error of judgement; a Caesarean section under local anaesthesia should have been performed. Actually, the patient was given a trial of labour; but early in the second stage she collapsed and developed alarming symptoms of heart failure with pulmonary oedema. After an anxious six hours her condition improved, and in consultation with Dr. J. L. Grove I gave her a low spinal anaesthetic and tried "high forceps" delivery. This failed, and in view of the mother's serious condition I performed a craniotomy and was able to make a quick delivery. The cord was injected at once, and the placenta was immediately expressed, with very little loss of blood.

In the eighth case the patient was the pre-eclamptic mentioned earlier, who had a partial placenta accreta.

Discussion.

It is not suggested that cord injection should be employed as a routine measure. The usual expectant treatment in the third stage should always be employed; but in certain cases the procedure should be used in anticipation of trouble, as in threatened uterine atony or after intra-uterine manipulations in the second stage. It was tried in a number of cases in this series to test its value in checking post-partum haemorrhage, and I am of the opinion that Currie's claims are justified. I believe that the value of the method is increased when the temperature of the saline solution is raised above blood heat, as suggested; rapid injection of hot saline solution is a much more effective way of stimulating the uterus to contract and of stopping haemorrhage than a Cr  d   manoeuvre, and it causes no shock. If there are any disadvantages in the method, they were not apparent in the present series. In the majority of these cases delivery was normal, but the third stage was unduly prolonged or haemorrhage was abnormally severe. The injections were given before this blood loss became excessive and in preference to repeated attempts at Cr  d   expression.

If the apparatus is ready to hand in the labour ward, it takes only a few minutes to carry out the injection, and in many cases the results are dramatic. In certain cases, it can be considered a life-saving measure, and in others it decreases blood loss and shock. In itself, it does not cause morbidity during the puerperium. In my opinion, the method should be taught in detail to all students during their obstetric training. The technique can be satisfactorily learnt by practising on the placenta after delivery. Students should be advised to have the simple apparatus

necessary for the operation in their obstetric bags, ready for use when required, so that the patient can at least be given the benefit of a trial of the method before she loses an abnormal amount of blood, before shock is caused by repeated efforts to expel the placenta and before a manual removal is carried out.

Summary.

1. Attention is drawn once again to the value of the Mojon-Gabaston cord injection technique in the treatment of retained placenta and post-partum haemorrhage.

2. The technique of the procedure is briefly described, emphasis being laid on the importance of using hot saline solution for the injection.

3. The results of using the method in a series of 51 cases are discussed and briefly analysed. Morbidity after the procedure was rare, and occurred only when interference of some kind had been necessary.

4. More extensive use of this simple procedure is recommended, especially in cases of steady haemorrhage from an atonic uterus, and as a prophylactic measure when trouble in the third stage is expected. Inclusion in the teaching curriculum of the technique and application of this method is strongly urged.

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Reports of Cases.

HIRSUTISM OF ADRENAL ORIGIN.

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Clinical Record.

A SINGLE woman, aged twenty-four years, was admitted to Lewisham Hospital under my care in March, 1942, for investigation of the cause of excessive hair particularly on her face and neck (Figures I and II). The hirsutism had been first noticed five years earlier, and she had been under the care of a "hair removal specialist" during the previous eighteen months; but the patient stated that the hirsutism was now worse than when she had commenced treatment. She had never suffered from headaches and had gained two pounds in weight during the preceding six months. Her menstrual history was in no way abnormal; the periods were regular on a twenty-eight day cycle and lasted for three days, and she used three or four diapers a day; but her mother considered her monthly loss to be "scanty". Her general health was and had always been good. There was nothing noteworthy in her personal or family history.

Examination revealed that the systolic blood pressure was 100 to 140 millimetres of mercury and the diastolic 70 to 90. The hirsutism was pronounced on her face, neck and chest, also on the areola of her breasts and on the proximal digits of her great toes, and the distribution of her pubic hair was male in type. Otherwise the physical findings were normal. The pulse rate varied between 74 and 96 per minute.

A tentative diagnosis of glandular dystrophy was made, and in the differential diagnosis the following conditions were considered: basophilic adenoma of the pituitary, arrhenoblastoma of the ovary, cortical tumour or hyperplasia of the adrenal, a tumour of the pineal gland, and thymus gland tumour. To arrive at a more precise diagnosis a number of investigations were carried out. An X-ray picture of her pituitary fossa was made. The radiologist's report was as follows: "The pituitary fossa is normal in size and there is no erosion of the clinoid processes." The report after excretion urography had been carried out was as follows:

"In the plain skiagram there are no shadows suggestive of calculus. Both kidneys are excreting the dye. On the left side there is a marked dilatation of the renal pelvis but no clubbing of the calyces. There is probably a partial obstruction at the junction of the pelvis and ureter, possibly an aberrant vessel. Appearances in the right side are normal." On examination of the blood, the hemoglobin value was estimated at 86%; the red blood cells numbered 4,640,100 per cubic millimetre and the white blood cells 9,400 per cubic millimetre; the differential leucocyte count revealed no abnormality. The blood urea nitrogen content was 18 milligrammes per 100 cubic centimetres of blood, and the blood sugar content was 131 milligrammes per 100 cubic centimetres of blood. In the urine no albumin or sugar was found, and microscopic examination of the urine revealed one red cell, an occasional white cell, a few epithelial cells and some debris. The urine was sterile. Examination after a test meal revealed diminished acidity and hypochlorhydria. A glucose tolerance test gave the following results: before

The increase in the 17-ketosteroids based on the work of Crooke and Callow appeared to favour the assumption that the patient's syndrome was due to a tumour or hyperplasia of the cortex of one or both of her adrenals. The excretion urograms excluded the possibility that a large adrenal tumour might be displacing one of the kidneys downwards. The inflation of the perirenal areas with gas according to the method of Cahill was considered, but was omitted; I have been informed that the injection has been associated with some mortality.

The possibilities were placed before the patient and her mother, and they chose to accept the risk of operation. Accordingly on May 17 I decided to explore the abdomen through a subcostal incision as recommended by Cahill, as this approach gives a ready opportunity of palpating the ovaries as well as both adrenals. Arrangements were made to have several blood donors ready, in case adrenal insufficiency should develop after the operation, and for three or four days beforehand the patient was given gelatine



FIGURE I.

the administration of glucose, 60 milligrammes per 100 cubic centimetres; half an hour after, 95 milligrammes; one hour after, 181 milligrammes; one and a half hours after, 140 milligrammes; two hours after, 138 milligrammes. During the test the urine showed no evidence of sugar. The basal metabolic rate was -39%, and the patient weighed seven stone one pound. The blood cholesterol content was 90 milligrammes per 100 cubic centimetres. An Aschheim-Zondek pregnancy test gave negative results. An assay of the 17-ketosteroids in a forty-eight hour specimen of urine, collected by in-dwelling catheter on March 31 and April 1, was made by Dr. Victor Trikojus, who gave the following report: "Specimen, 31.3.42 (48 hours), vol. 1,840 ml., 17-ketosteroids, 19.9 mg. per litre, i.e., 18.3 mg. per 24 hours." The visual fields and fundi were normal.

The patient was examined per vaginam under general anaesthesia. It was found that her labia majora were enlarged, but the clitoris was not hypertrophied. The hymen was unruptured. The uterus was normal in size and position, and no mass was palpable in either fornix; her ovaries were palpable, but not enlarged. This finding was considered to be evidence in favour of the elimination of arrhenoblastoma from the differential diagnosis.



FIGURE II.

capsules containing 15 grains of sodium chloride three or four times in the day. The ovaries on palpation were of normal size and consistence and contained no large cysts. As the patient was thin, it was easy to palpate both adrenals through the posterior part of the peritoneum. To the palpating fingers they appeared to be about equal in size, and no swellings were palpable in them. However, with the knowledge of the increase in the amount of 17-ketosteroids in the urine, it was decided to remove the right adrenal. This was done without any technical difficulty, and the subcostal incision gave an excellent approach. An appendix which was subhepatic in position was removed to save possible later embarrassments for both surgeon and patient. The patient stood the operation well; her blood pressure at the end of operation was 120 millimetres of mercury systolic and 100 diastolic. The continuous intravenous drip administration of glucose and saline solution was started during the operation and continued for four days; three transfusions each of 500 cubic centimetres of blood were also given through the same needle during this period. Dr. F. B. Byrom was kind enough to undertake the pathological examination of the excised adrenal gland and his report was as follows:

Macroscopic.—The specimen consisted of several pieces of adipose tissue containing fragments of suprarenal gland. On section, the glandular fragments showed a uniform thickness of 0.3 centimetre and were composed of an outer zone of yellowish white lipid tissue and an inner blurred sepia coloured pigment zone. No medullary tissue could be detected. The gross appearances suggested that the cortex as a whole was, if anything, slightly thinner than normal. Blocks were taken from two portions of the gland and embedded in paraffin. Sections were stained with Ehrlich's hematoxylin and eosin and with Vine's ponceau fuchsin stain.

Microscopic.—In the *zona glomerulosa* and *fasciculata* the cells are stuffed with fat vacuoles and cytoplasm is limited to an inconspicuous reticulum. In the cells of the *zona reticularis* on the other hand, fat vacuoles are very sparse and the cytoplasm is abundant, being composed of confluent coarse granules which stain deeply with eosin. The nuclei in all three zones are circular or oval, with clearly defined chromatin network and single eccentric nuclei.



FIGURE III.

The contrast between the deeply stained *zona reticularis* and the paler outer zones is very conspicuous. This deeply stained zone accounts for slightly less than one-half of the total cortex. In one section stained by Vine's technique, the eosinophilic granules of the *zona reticularis* are deeply stained with ponceau fuchsin. In the other section, however, red staining is limited to red blood corpuscles. As a specific stain for the granules fuchsin does not appear, in this instance, to display any advantage over eosin.

Medullary tissue was scanty, being limited to a few narrow strands in the centre of the gland.

Comment.—The impression is gained that there is a hyperplasia of the alleged androgenic cells of the innermost layer of the cortex, at the expense of the outer layers of "adult" cells. In the absence of control tissue removed at operation from a normal subject of the same age and sex, a more positive opinion would be unjustified. Post-mortem material would not be satisfactory for purposes of control.

The patient was discharged from hospital on June 21. Figure II is a photograph of her taken two months after the operation.

The patient's convalescence was uneventful except for a slight wound infection. On April 4, 1942, most of the hair from her face was removed. It came away readily without any discomfort. Urine collected on June 16, 1942, during a forty-eight hour period was assayed by Dr. Trikojus with the following result: Specimen 16.642, vol. 2,130, 17 ketosteroids, 8.0 mg. per litre, 10.9 mg. per 24 hours.

Change in colour of the skin of the face was, after the loss of hair, one of the most striking alterations.

Comment.

In his book "Genital Abnormalities and Hermaphroditism", published in 1937, at page 230 and 232, Hugh Hampton Young has made the following statements:

The embryonic bisexuality of the gonad is manifested in the coexistence within it of the Müllerian and Wolffian ducts. Each organ of one sex has its counterpart in the other. Later in embryonic life in the female the Müllerian ducts develop greatly while the Wolffian are



FIGURE IV.

partially absorbed, and vice versa in the testicles. The external genital organs are in reality only degrees of the same evolution, each organ of one sex having its counterpart in the other, e.g. the penis and clitoris, the prostate and the paraurethral glands of Skene being homologous. The differentiation of the androgenic tissue of the adrenal as a unit distinct functionally from the remainder of the adrenal cortex explains the fact, according to Grollman, that adenoma or carcinoma of the cortex proper do not give rise to abnormalities of the reproductive system. The view advanced is in accord with all the known facts, and permits one to account logically for the adreno-genital relations, and avoids the previous chaotic confusion in trying to account for the relation between the adrenals and the reproductive system. Grollman divides adrenal gland into three functionally distinct tissues, (1) chromaffin (medulla), (2) inter-renal (cortical), and (3) the androgenic, which differs anatomically and histochemically from true cortical tissue, and which is normally only temporary in its existence. The cortex proper, although

essential for the well-being of the sex glands, neither controls them nor does it, by hyperactivity, produce any demonstrable changes in the reproductive system.

Histology.

The medulla belongs to the chromaffin system, which comprises a number of organs, some minute in size, which are serially arranged on both sides of the aorta, most of them in close proximity to the sympathetic ganglia. To the chain of these paraganglionic bodies belong the carotid bodies, the paraganglia proper, and the aortic bodies, and in part the medulla of the adrenal glands, which form the larger and further developed paraganglia.

We are not interested here in this complex system, but more in the cortex of the adrenal and aberrant adrenal rests, which are found adjacent, and even in the remote pelvis. These may be of such size as to form accessory adrenals, and play an important part in the adreno-genital syndrome.

The histology of the adrenal is graphically shown in figure 156. Lack of space prevents further description. Besides the cortical, or inter-renal and the medullary, or chromaffin tissue above referred to, one finds a third type of tissue, which has been designated as embryonic boundary zone, fetal or X-zone, but which is referred to also as the androgenic tissue. This tissue differs from the remainder of the cortical tissue, not only in its morphological and histochemical properties, but also in the fact that it normally exists only during a certain period of life. Hypertrophy of this tissue, under certain pathologic conditions in man, may give rise to a symptom complex, characterized by masculinisation of the female. Because of this property, Grollman has designated this tissue as androgenic. He admits that experimental evidence needs to be produced to prove definitely the exact relation of the function of the androgenic zone to the reproductive system, but he thinks that the facts at hand suffice to indicate, as already stated, that the cortex comprises two tissues, one of which—the inter-renal—produces the hormone, which is essential to life, and the other—adrogenic tissue—which has as yet some incompletely defined function relating to the reproductive system. This androgenic tissue develops during fetal life, and disappears almost entirely during the first year of life (Elliott and Armour). Goldzieher, as previously stated, described an abnormally thick layer of the reticular zone (figs 150, 151 and 152) which stained densely with eosin, and Broster and Vines speak of the fuchsinophilic reaction of cells in this same zone which corresponds to the androgenic zone of Grollman.

In early embryonic life the adrenal is larger than the kidney, and at birth one-third as large. This is due to the presence of a thick zone separating the true cortex (inter-renal tissue) from the medulla. Grollman, to whose book we are much indebted, considers this the same tissue which he has designated the androgenic zone, and a glandular entity, specific in its function, and to be differentiated from the rest of the cortex.

Accessory adrenals, which are found beneath the lower pole of the kidney along the internal spermatic artery, on the ileo-psoas muscle, in the solar or renal plexus, between the transverse colon and the spleen, in the liver and pancreas, and adjacent to the reproductive organs, have in the past been described as accessory cortical tissue, but they are composed of androgenic tissue, and completely independent functionally from the cortex proper and from true adrenal cortical accessory bodies. This accessory adrenal tissue, common at birth, disappears during infancy simultaneously with the androgenic zone of the adrenal, but in cases of hermaphroditism it persists. Later in life this androgenic tissue may give rise to tumours, which in the female cause adrenal virilism. These masses of accessory androgenic tissue are also found along the spermatic cord between the testis and epididymis, and in the rete testis and paradidymis. It is found on the Fallopian tubes, in the broad ligament, and in ovaries in a large percentage of all new-born females. The post-natal involution of this, the androgenic zone, was first described in 1911 almost simultaneously by Elliott-Armour and Kern.

In the embryo of eight weeks the adrenal lies anterior and in contact with the kidney. The two organs at this stage of development are of equal size. The peripheral cells are filled with lipoids and represent the cells which will subsequently form the cortex of the

adult adrenal. The central part of the glands is composed of larger, angular cells filled with granular cytoplasm. These cells, which are loosely arranged, constitute the androgenic zone of the adrenal. During most of the period of intrauterine development the true cortex remains as a comparatively thin rim of closely bound cells with deeply staining nuclei. The androgenic zone grows rapidly and forms the main bulk of the gland. At birth the true cortex has assumed its division into definite zones. The androgenic zone begins to involute after birth, and this involution continues during the first years of life. It is not until the third year that the gland assumes the appearance of the adult gland. The androgenic zone in the new-born is very vascular. Soon after birth involution begins, and the cells are found in all stages of differentiation. The differentiated androgenic zone is sharply demarcated from the true cortical tissue, which remains intact and distinct from the growing medulla. At the end of the first year this zone is replaced with connective tissue, in which may still be found differentiated pigment cells. Lewis and Pappenheimer also showed the simultaneous disappearance of the accessory cortical tissue or accessory androgenic bodies, as Grollman calls them, and which he thinks is evidence for their physiological homology with the androgenic zone of the adrenal. He believes the androgenic tissue may remain throughout life as a small group of cells which hypertrophy when the female reproductive system undergoes fundamental changes, and that when this hypertrophy becomes pronounced, the adreno-genital syndrome results, and is responsible for the changes in the reproduction system which are associated with tumors of the adrenal. The true inter-renal or cortical tissue seems not to be involved in the genesis of these disorders.

In the same work, at page 213, Young states: "We have found 36 cases of adrenal hyperplasia among adult females." After operation in this group of cases "the hirsutism entirely disappeared in 3 cases, it was distinctly less in 15 cases and no change was noted in 1 case".

Acknowledgements.

The patient's and my own thanks are extended to Professor C. G. Lambie, of the Department of Medicine, University of Sydney, for placing the facilities of the department at our disposal; to Dr. V. M. Trikojus for his estimations of the 17-ketosteroids in patient's urine before and after operation; to Dr. F. B. Byrom for his interest and pathological report on the tissue removed; and to Mr. Woodward Smith, of the New Medical School, University of Sydney, for the photographs.

Notes on Books, Current Journals and New Appliances.

REGIONAL ANATOMY.

THE atlas of regional anatomy, by E. B. Jamieson, Senior Demonstrator and Lecturer in Anatomy of the University of Edinburgh, is well known and widely appreciated. The third edition was noted in these columns in May, 1941; the fourth edition has now appeared.¹ The third edition of Sections I to V, we are told in the preface, had had barely six months of life and some copies of the last edition of Sections VI and VII were still in hand "when a disaster befell them all, together with many other educational works". It became necessary to print again and with all speed. On account of scarcity of paper and shortage of printing staff—conditions not unknown in this country—there has been a delay. In these days of wartime surgery an atlas of regional anatomy is more welcome than ever and there will no doubt be a keen demand for the present edition. The chief improvements in this edition consist in an increase in the number of coloured illustrations. Into the fourth edition of Sections I to V 163 new colour blocks have been introduced; in the third edition of Sections VI and VII 79 have been added. One or two of the plates have been enlarged and some extra plates have been added. The nomenclature employed is that approved by the Anatomical Society at Birmingham in 1933; where the names differ radically from the Basle Nomina Anatomica ("B.N.A.") these names have been added. This atlas can be recommended to both students and practitioners.

¹ "Illustrations of Regional Anatomy", by E. B. Jamieson, M.D.; published in seven sections; Fourth Edition: 1942. Edinburgh: E. and S. Livingstone. Foolscap 4to.

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Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

AN INVESTIGATION OF CHRONIC PULMONARY DISEASE IN COALMINERS.

Most people know that the hazards associated with coal mining are many and varied; those who do not appreciate this fact will not be long in doubt if they will turn the pages of the report of the Royal Commission appointed in New South Wales in 1938 to inquire into and report upon the safety and health of workers in coal mines. The Commissioners, Mr. Justice Davidson, Mr. S. McKenzie and Mr. F. Lowden, produced a document which covers every aspect of the subject. One of the sixteen sections is devoted to health matters and gives a first-rate review of the literature on pulmonary disease in coalminers and of the views of Australian workers. This report should be more widely known than it is. No one will deny that the prevention of pulmonary disease in coalminers will be possible only if its pathogenesis is understood. There are still many gaps in our knowledge and for this reason industrial hygienists have turned hopefully to a new report which has just made its appearance.

The present report which has been issued as one of the "Special Report Series" of the Medical Research Council of Great Britain has been called "Medical Studies". It is really only the first part of the whole report. The problem, we are told in the preface, is twofold. First there is the question of the nature of the pulmonary diseases and their occupational and geographical distribution in the south Wales Coalfield; it is this with which the present "Medical Studies" deal. The second part of the problem, that of the environmental conditions concerned in the causation of the disease and of whether improved preventive measures might be made possible by better knowledge of these conditions, will be dealt with in a second volume. It

is perhaps important to point out that the field investigations for this report were started in December, 1937. The work was still in progress when war started in 1939. The decision to complete the programme of work is typical of British doggedness. The field investigations were completed early in 1941 and since then time has had to be spent in the collation and assessing of the evidence obtained. The date of the preface is February 28, 1942, and at this stage of the war the present book of 235 pages, with its superb reproductions of skiagrams and photomicrographs, and dealing with a subject of general preventive medicine, makes its appearance. This must be regarded as a valuable object lesson to certain governmental authorities in Australia whose sense of values in regard to publications does not always appear to be particularly keen.

The conditions which led to the investigation were, first of all, that an increasing number of cases certified as silicosis were coming from the anthracite area of the south Wales mines, and secondly, that there existed among south Wales coalminers a disabling pulmonary disease, apparently due to employment, but which did not come within the definition of silicosis. It was clear that the condition designated silicosis in south Wales differed in certain respects from the type which results from exposure to dust containing a high proportion of quartz. In order to ascertain beyond doubt the relation of incidence to type of occupation, it was decided to make first of all a radiological and clinical investigation of the entire population at one colliery in the anthracite area, the records of which showed a high incidence of silicosis. In this instance 560 men were examined and it soon became apparent that the collier working at the coal-face provided the fundamental problem. In the subsequent investigation 1,392 colliers from mines in south Wales, both anthracite and non-anthracite, were examined radiologically and an occupational history was taken. In addition 470 coal-trimmers working on ships were examined in the same way, as well as 33 long-term workers on the surface screens and 60 hauliers from two bituminous coal mines. On the result of all these examinations the conclusions in the report are drawn. As a matter of fact the actual report, which is issued by the Committee on Industrial Pulmonary Disease, forms only a kind of introduction to the work. The "Medical Studies" proper are divided into two parts—a medical survey, by P. D'Arcy Hart and E. A. Aslett, and a pathological report by T. H. Belt and A. A. Ferri. The ground covered by this important investigation is so extensive that it will be possible in the present instance to discuss only the main features which call for comment.

The methods of examination used by Hart and Aslett comprised a radiological examination, a clinical examination and the taking of a working history. In addition lung volume determinations were made in some cases and a tuberculin test was applied to a sample group of men. The order in which the methods of examination are placed should be noted. Most people would put the first three in the reverse order, but Hart and Aslett believe that in "assessing a man" exposed to a dust hazard, "the X-ray" (presumably the skiagram is meant) should be used as the chief index of the anatomical presence and degree of progression of the pulmonary condition, and that the clinical findings should be recorded separately, as

¹ "Chronic Pulmonary Disease in South Wales Coalminers: I. Medical Studies", Medical Research Council of the Privy Council, Special Report Series, Number 243; 1942. London: His Majesty's Stationery Office. Royal 8vo, pp. 236, with illustrations. Price: 10s. 6d. net.

indicating the disability and constitutional effect produced by the condition. They have used a radiographic classification, rather than a combined clinical and radiographic classification, as the primary basis for grouping the subjects examined. They devised a classification for what they call their X rays and have termed the categories: (a) normal, (b) reticulation, (c) nodulation, (d) coalescent nodulation, (e) massive shadows, (f) multiple fluffy shadows, and (g-h) indefinite. Categories (c-f) are grouped under the heading "consolidation", and categories (d-f) have been called "major consolidation". It is necessary here to give a short description of these X-ray appearances; they are illustrated in the report in a series of well-reproduced skiagrams. In the so-called normal films the lung fields are normal, but films with homogeneous or patchy shadows at one or both apices are included in this category. In the films showing reticulation the lung fields are marked by a fine network, sometimes sharp and lace-like in pattern, but much more often blurred in appearance. The network occupies from half of one lung field to the whole of both fields, though the apices are relatively free. It is to be noted that the markings are just as prominent in the peripheral areas as they are in the vicinity of the hilum. In X-ray films showing nodulation multiple discrete shadows, from two to five millimetres in diameter, are present in a considerable number in each rib space; they may extend over the whole of both lung fields, when they give a "snowstorm effect" to the picture. The term coalescent nodulation explains itself and massive shadows are often symmetrically distributed and often associated with well-marked emphysema. Hart and Aslett give a résumé of previous classifications of X-ray appearances. They point out that there are many variations, that these other classifications agree broadly in describing discrete nodular shadows and conglomerate or coalescent shadows, but that it is uncertain whether and how far the various descriptions of linear shadows correspond with what they have described as reticulation. They also discuss reticular X-ray patterns mentioned by previous authors. These have dealt mainly with silicosis, which is thought possibly not to be relevant to the present discussion. However, among the authors mentioned is Sampson, who discussed "marked linear exaggeration". Sampson thought that their appearance might be caused by prolonged exposure to various dusts and that with some of these dusts it possibly preceded nodulation. He also held that this appearance might occur in unexposed persons and that in them it might be due to age, chronic infections, cardiovascular disease or even faulty technique. Sampson held further that even in dusty occupations this linear exaggeration showed no very clear relation to the duration of exposure. In regard to observations made in the coalmining industry, Hart and Aslett refer to the work of Amor whose X-ray atlas of silicosis was published in 1941. They write: "According to this author, linear changes are most definite in industries in which the silica content of the inhaled dust is high and the total quantity of dust considerable, while reticular changes tend to be more marked among anthracite miners than in men subject to classical forms of silicosis. Amor regards both linear and reticular X-ray changes as non-specific, in the sense that with advancing age they are not uncommonly found in the normal town-dweller, as well as in the workman whose

occupation exposes him to other dusts besides those associated with the production of silicosis." Hart and Aslett compare their views with those of these previous authors. If these authors recognize a reticulate change, they do not stress it as an essential part of the pneumokoniotic process, whereas "we hold that reticulation is as characteristic a feature of the pneumokoniosis of coalminers as the discrete and conglomerate shadows, and that it may even have as specific a causation". This last is surely unnecessary when they have described appearances of reticulation and nodulation in the X-ray picture as successive stages of the one process. At this stage exception must be taken to the careless way in which Hart and Aslett have expressed many of their ideas. What they have described as reticulation and nodulation are merely appearances seen on a photographic film taken with an X-ray machine. They do state that "reticulation, nodulation and consolidation are used purely descriptively" and to this is added: "although it happens that they correlate with a fairly well-defined pathology". As we shall see later a condition of "dust-reticulation" is described in the section on pathology by Belt and Ferris. Hart and Aslett, all the way through their long contribution, refer to the shadow as though it was the substance. The reader has to be continually on his guard and to remind himself of this. We read: "The incidence of reticulation among colliers varies considerably from one mine to another." Again: "Like consolidation, reticulation is produced most frequently in certain anthracite mines, and the incidence is lowest in the mines of the bituminous area." It is fibrotic or other change which is produced in the lungs of men working in a certain mine; what Hart and Aslett call reticulation is produced on a photographic film. Reticulation is not found lying about in mines, as might be justly assumed from: "In no mine of the series examined has reticulation been entirely absent." The cream of the offerings must surely be in the following remarkable product: "The majority of colliers who develop reticulation on the X-ray will have progressed to consolidation before the end of a normal working life"—Consolidated Miners, Limited! After this necessary digression mention must be made of the correlation of respiratory disability with the appearances found on X-ray examination of the lungs. It was found that in regard to respiratory disability men whose skiagrams showed reticulation occupied a position between those whose skiagrams were normal, and those whose skiagrams showed evidence of consolidation. This position, however, was not much below that corresponding to the nodulation component of the latter composite category, but was considerably below that of its more advanced component, major consolidation. The incidence of disability among those whose films showed reticulation fell mainly on men in the second half of life, but in many instances no clinical symptoms were present at all.

In their pathological report Belt and Ferris record their findings on the examination of material from nine persons who died from intercurrent disease or as a result of accident and whose lungs during life gave on X-ray examination the appearances of reticulation. The changes were such as would ordinarily be described as simple anthracosis, but Belt and Ferris, like many other workers in this field, look on this designation as unsuitable. One of their reasons for rejection is that to most persons the

term anthracosis signifies a harmless state of pigmentation like tattooing of the skin; the condition which they wish to describe "seems to have definite pathological features". They have therefore adopted tentatively the non-specific term dust-reticulation. They state that the word reticulation has come into the terminology of pneumoconiosis by radiological channels and that it is "by coincidence" also applicable to the corresponding histological changes. The dust deposits, they explain, are scattered in a lace-like pattern of fine streaky processes throughout both lungs in a way corresponding to the diffuse lattice-work shadows seen on X-ray examination. The change is diffuse and symmetrical and affects all parts of the lung more or less uniformly, with the exception of the extreme base, where it is often less pronounced than elsewhere. "The distribution is essentially that of the lymphatic pathways and depots." The root glands are packed with dust; in the lung itself there is a heavy storage along the interstitial tracts in the perivascular and peribronchial sheaths as well as in the interlobular septa and subpleural tissues. Under the high power of the microscope the collections are seen to be distinctly patchy with a tendency towards localized concentration. They look like dust-ridden cobwebs, all linked up one with another, more or less in continuity or in series. They represent traps where dust-laden phagocytes have been brought to rest and transformed into fixed-tissue phagocytes which then become knit together into a mesh-work by the elaboration of reticulum fibres. The condition is actually a form of fibrosis, but we are reminded that the fibres are reticular, of very fine calibre and of loose mesh. It is quite different from collagenous fibrosis; the term fibrosis "commonly connotes collagenous connective tissue and in that sense it is not applicable to dust-reticulation". The process involved is analogous to tattooing in that it is a permanent storage of particulate matter by fixed macrophages. The tissue response is almost exactly proportional to the amount of foreign particles; there is no redundancy of reaction, and in this it is unlike silicosis in which there is a disproportion between the amount of fibrosis and the amount of dust. In other words there is something more complex about the silicotic reaction. Later on, when confluent fibrosis develops, a collagenous fibrosis of greater or less degree is added, and the question arises whether this fibrosis is the result of coalescence of smaller lesions or whether the process is diffuse from the start. Of course, before the stage of confluent fibrosis there is nodular formation, and Belt and Ferris describe nodules of three types—the silicotic nodule, the nodules of nodular reticulation and a mixed nodule, which is the commonest. The formation of cavities is another process that should be mentioned. Belt and Ferris thus describe three main pathological processes which have to be considered—dust reticulation, silicotic fibrosis and koniophthisis. They consider each of these in turn in an attempt to assess the aetiological factors. They conclude that there is good evidence for regarding the dust-reticulation of colliers as due more to the action of silica than coal (they use the term silica to include silicates as well as free silica). While we may admit that this is probably correct we have to remember, as Badham has recently stated in this journal, that in the pit in New South Wales in which most cases of coal-miner's lung occur, the coal contains only 0.5% free silica.

He also pointed out that the presence of free silica is not the only necessary factor, since shale dust, which contains a high percentage of free silica, does not cause silicosis. As a matter of fact Belt and Ferris claim the paradoxical finding that silicotic fibrosis contains less silica (according to their nomenclature this includes silicates and free silica) than is present in dust-reticulation. They see in dust-reticulation and silicotic fibrosis two different forms of silica effect; and further, silicotic fibrosis is a sequel to dust-reticulation, but not an obligatory one. To explain the sporadic progression of one to the other they postulate an unknown sporadic factor "X".

When in a subject of this kind we reach a stage of postulated unknown factors it is time to call a halt, at least for the time being. This whole report put out by the Medical Research Council, full as it is of suggestive detail, must be carefully considered by every student of the subject, in spite of the fact that it really does not take us much further on the road to ultimate discovery. Fundamentally we are perhaps not much nearer the final goal than we were in 1939 when Charles Badham, who has found in New South Wales the same selective pulmonary involvement in different mines as has been found in south Wales, published in the Report of the Director-General for Public Health the results of his second investigation in coalminer's lung. On that occasion he stated that if the dusts aggregated at the pulmonary lymphatic nodes were of active free silica—free silica unmodified by other dusts—the typical silicotic response appeared; if the dusts consisted of free silica inactivated by other dusts or was modified in its action by so-called inert dusts, the response would not be that of the silicotic type. He thought that no early answer was likely to be forthcoming to the question of how far the non-silicotic type of reaction was due to the inert dusts and how far to the minimal amount of free silica found with the inert dust. In other words it remains to be seen whether the series of changes described by the English investigators and illustrated in their radiological adventures will provide a jumping-off ground for a further advance. In the meantime every industrial hygiene worker in this country will agree with the declaration of the New South Wales Royal Commission, already mentioned, that intensive scientific research should be devoted to this subject.

Current Comment.

TAPEWORM INFESTATION FOLLOWED BY DEATH.

A CASE of unusual interest has been reported by Sir Arthur Hurst and A. H. T. Robb-Smith.¹ A woman, aged fifty-two years, was admitted to hospital in *extremis*; she died with symptoms of enteritis and at autopsy a living tapeworm, *Tania saginata*, was found in the lower part of the duodenum and in the jejunum. The case is described as one of fatal tapeworm enteritis. Infection by *Tania saginata* is generally supposed to cause no symptoms in man, except perhaps some diarrhoea or constipation. The history of the patient described by Hurst and Robb-Smith is therefore worthy of detailed consideration. They state that the only record they have been able to find of a case which in any way resembled their own was one recorded by Loeper in 1931. A girl, aged six years, suffered for

¹ *Guy's Hospital Reports*, Number 1, 1942.

four years from severe diarrhoea, which was often "serous" and which showed no response to any form of dietetic or drug treatment. Eventually she was found to be infested with *Tania saginata* and complete recovery followed expulsion of the worm.

When Hurst and Robb-Smith's patient was admitted to hospital, she was semi-conscious and unable to give any account of her illness. She was stated by her medical attendant to have suffered from diarrhoea for seventeen years. The stools had been watery and contained neither blood nor mucus. In spite of her disability, the patient carried on until two months before her admission to hospital, when she went to bed. After slight improvement her condition rapidly became worse. She became extremely emaciated and was in a condition of severe dehydration. She became incontinent of urine and faeces, was comatose and died nine days after her admission to hospital. At post-mortem examination the first part of the duodenum appeared normal. The third part and the whole of the jejunum were acutely inflamed, but not ulcerated. Microscopic examination revealed a congestion and infiltration of the mucosa with cells, many of which were eosinophile. Lying in the lower part of the duodenum and in the jejunum was a living *Tania saginata*. The upper part of the ileum was normal; the lower part was considerably thickened, but no gross abnormality was found on microscopic examination. The whole of the colon was greatly thickened, and there was much fibrosis in the wall. The mucosa was smooth and granular, and multiple polypi were present. There were no erosions. Microscopic examination revealed loss of mucosa and fibro-muscular hypertrophy. The polypi were glandular adenomata. Considerable lymphoid and eosinophile infiltration was present. The rectum was healthy. The liver showed diffuse atrophy, but no other abnormality. It was after the post-mortem examination that the patient's husband remembered that she was supposed to have suffered from tapeworms twenty-five years previously; he added, however, that nothing had occurred since then to suggest that the infestation was still present.

On the face of it, this case would appear to be one of fatal tapeworm enteritis, as Hurst and Robb-Smith suggest. It would be well, however, to accept this diagnosis with caution. That no reference to severe enteritis in the literature could be discovered by Hurst and Robb-Smith merely serves to emphasize the need for caution. Signs of acute inflammation were present in the duodenum and jejunum, but the upper part of the ileum was normal. The colon again was the site of abnormalities which could give rise to diarrhoea and which are often found apart from *Tania saginata* infestation. It is unfortunate that but little appears to have been written about the pathology of *Tania saginata* infestation.

CONGENITAL FLAT-FOOT.

In no regard does man display more fatalism than in his attitude towards himself. Perhaps complacency describes it better than fatalism. Fortunes have been spent in attempts to grow a black tulip or a blue rose, in improving the breed of sheep or cattle, in developing rust-proof wheat, or producing unbeatable racehorses. Few attempts—and those mostly misdirected—have been made to improve the strain of *Homo sapiens*, or to produce a race that is free from deformity and proof against disease. Perhaps that is impossible. However it be, one must welcome accurate and critical descriptions of prevailing defects. It is only by seeing ourselves as we really are, as a race, that the foundation for future improvement can be laid. And, after all, what better foundation can a man have than a pair of perfect feet? More especially when petrol, railway travel, bicycles, boots, shoes and other artificial aids to getting about are curtailed or rationed.

And so we should ponder, in all seriousness, the statement by John G. Kuhns that weakness and other

disturbances of the feet are found in more than 50% of all small children. Many of these disturbances disappear spontaneously as the child develops better balance and skill in walking. But a small number show persistent ligamentous relaxation, with displacement of the medial tarsal bones inward and downward on weight bearing. Patients with milder deformity often show generalized relaxation of the subcutaneous tissue and of ligamentous structures; they are, as the saying goes, "double-jointed". Kuhns maintains that, whether mild or severe, cases of "congenital flat-foot" all progress and lead to serious disability if the condition is not treated. In infancy and early childhood congenital flat-foot can be diagnosed primarily by the extreme ligamentous relaxation about the foot. Examination of the depression of the arch on weight bearing is, of course, of no assistance before walking is well established. Walking by these children is often delayed. There is defective balance and great awkwardness and shoes become misshapen rapidly. An interesting point is that heredity seems to play a part in the causation of congenital flat-foot. Kuhns states that in every instance in which a careful inquiry was made, a similar disability was found in the family of one or both ancestors. Sufficient data are not yet available, but what evidence there is suggests that the condition behaves like a recessive trait. No evidence has as yet been brought forward of any nutritional disturbance in these children, but treatment, to be effective, must commence in early childhood; and adequate nutrition and sufficient rest and exercise are prerequisites. The foot should be held while at rest and in weight bearing in inversion and with slight elevation of the dorsal arch. Kuhns emphasizes the fact that half-hearted measures are ineffective. When the flat-foot is not corrected by the methods he describes, relief of symptoms can be obtained by proper shoes and by supports under the longitudinal arch and the inner side of the heel. No operative procedures, in his opinion, should be undertaken, even when there is serious disability, before the age of twelve years. As Lapidus said, in a discussion following the reading of this paper: "No plastic surgeon would attempt to reshape the nose of an eight or ten year old child, since at this age the facial features have not yet reached their permanent configuration. The same is true of the shape of the foot, yet not infrequently reconstructive operations for flat foot are performed in young children." Kuhns's descriptions of his method of treatment are clear and merit careful reading. But this treatment is a long and tedious business, and the reader's mind turns back to Kuhns's disturbing opening sentence: "Weakness and other disturbances of the feet are found in more than 50 per cent of all small children." Somebody should try to find out why. If they were small sheep, now, or small racehorses, someone would. Perhaps the best we can do at present is to stick to wrenching exercises and plaster casts.

NECROSIS OF THE LIVER FOLLOWING THE TANNIC ACID TREATMENT OF BURNS.

SINCE the outbreak of war a great many articles have been published in medical journals on the treatment of burns. In these articles reference has been made to the tannic acid treatment perhaps oftener than to any other form of treatment. The results of treatment with tannic acid ever since it was introduced by E. C. Davidson in 1925, have on the whole been remarkably good. It is only recently that for various reasons some workers have recommended the replacement of the tannic acid treatment by other methods in certain circumstances which need not be set out in detail at the moment. The pathology of burns is not completely understood, and one of the most interesting of the findings is necrosis of the liver which was first described by W. C. Wilson, A. R. Macgregor and

¹ The Journal of the American Medical Association, October 3, 1942.

² Surgery, Gynecology and Obstetrics, Volume XLI, 1925, page 202.

C. P. Stewart in 1938.¹ They referred to it as the most striking and characteristic feature of the pathology of burns, and they stated that it had not, as far as they could discover, received special attention in the past. They described it in two forms. In its earliest form, at about twenty-one hours after injury, it appeared as fatty degeneration of the epithelial cells surrounding the efferent veins in the central zone of the hepatic lobules; the fatty degeneration was accompanied by nuclear damage, especially karyolysis, which was constant and was more severe in proportion to cytoplasmic changes than in most other conditions which produce degeneration of cells of the central zone. At a more advanced stage, from fifty-seven hours onwards, the characteristic form of damage was found. On naked eye examination the liver was slightly enlarged, light yellow, soft, greasy and friable. On the cut surface the lobular marking was conspicuous owing to greater pallor of the central zone; sometimes, however, hæmorrhage in the central zones produced an appearance resembling a "nutmeg" liver. On microscopic examination necrosis of varying degree of the cells of the central parts of the lobules was seen. In the most extreme examples only a narrow strip of liver substance surrounding each portal tract showed surviving liver cells; the remainder were completely necrotic. D. B. Wells, H. D. Humphrey and J. J. Coll have recently drawn attention to this interesting condition in a paper read before the New England Surgical Society.²

These observers report that in ten consecutive autopsies following death from burns there were four cases in which death was due to toxæmia and occurred ninety-three to one hundred and twenty hours following the original injury. In each of these four cases central lobular liver necrosis was present as an "outstanding lesion" or as the sole cause of death. These patients were treated by immersion in tannic acid solution in a tub in which débridement was carried out without an anæsthetic; a thin "sterile tan" was secured in every case and the tan was subsequently maintained by use of a tannic acid spray. In the first case there was a combination of early liver necrosis and vascular failure; the latter was probably the greater lethal factor. In the second case changes suggestive of vascular failure were present, but the picture was dominated by liver necrosis. In the third case death was due solely to liver necrosis. In the fourth case the liver necrosis, which was more extensive than in any of the other three instances, was complicated by lobular pneumonia, inactive rheumatic heart disease and vascular failure. In view of these findings, Wells and his co-workers planned a series of experiments to investigate the role of tannic acid in the production of liver damage. They maintained albino rats on specific diets and gave them subcutaneous injections of 5% or 10% solutions of tannic acid. The rats were killed on the third or fourth day. Of 77 rats injected, eight failed to survive. Every one of the remainder showed some degree of liver damage which, in general, varied directly with the amount of tannic acid injected and the number of injections given. All other organs examined presented a normal appearance, except for a slight cloudy swelling. The liver damage was characterized by: (a) necrosis of the liver cells in the central portion of the lobule; (b) a variable zone of intact cells in the peripheral area exhibiting a granular cytoplasm and enlargement of the nuclei, with irregular clumping of hyperchromatic nuclear material; (c) regular and bizarre mitoses; (d) hæmorrhage and leucocytic infiltration, which were present in minor degree in areas of necrosis. Wells and his fellows illustrate their pathological and experimental findings with excellently reproduced photomicrographs; and it is clear that the changes produced in the animals were comparable to those seen in human patients. Stress is laid on the fact that the degree of liver damage produced experimentally was in direct proportion to the amount of tannic acid injected subcutaneously. Similar results have been obtained by the injection of rabbits and guinea-pigs with tannic acid.

When inquiry is made into the cause of a liver necrosis, attention is naturally focused on acute toxæmia. Wilson, Macgregor and Stewart hold that this acute toxæmia is distinct from septic or bacteriogenic toxæmia. In their opinion the only hypothesis which will explain both the clinical and pathological features is that of the action of a toxic principle which has been absorbed from the burned area. They point out that it is difficult to suggest any mechanism other than the action of a toxin which could produce the extreme degree of liver damage. They state that such grounds would be insufficient for the acceptance of the toxin hypothesis, were it not for the fact that animal experimentation is favourable to this view. They also refer to observations by Wilson, Jeffrey, Roxburgh and Stewart that toxin formation occurs in burnt areas and that it is the result probably not of bacterial action but of autolysis of burnt tissue. At this point it is of interest to refer to an important paper by T. H. Belt published in 1939.³ Belt reports four cases in which necrosis of the liver occurred in persons who died after burns accidentally received. In each of these instances tannic acid treatment had been used. He shows that the liver changes caused by toxæmia, in certain cases of burns, are similar to those observed in certain virus diseases, such as yellow fever, and this suggests to him that the noxious agent in both instances, whether it is a virus or a toxin, is of a similar character. Further, W. Irving Clark in the discussion that followed the reading of the paper by Wells, Humphrey and Coll drew attention to the fact that liver necrosis following burns resembled a condition produced by chloroform and also that inhalation of the fumes of chlorinated hydrocarbons gave rise to a similar necrosis. Clark remarked that it was not proved whether the toxæmia of burns was due to histamine or to some other substance. From his observations on chloroform and the chlorinated hydrocarbons, he gathered that the greater the amount of chlorine in the formula, the more pronounced and more acute was the necrosis. He thought that possibly tannic acid produced in the body a metabolic change resulting in hyperchlorination of the tissues. He admitted that this was purely a speculative suggestion.

The first point about the work by Wells, Humphrey and Coll is that care must be taken not to attach too much importance to the results of the injection of tannic acid into animals when the results of tannic acid treatment of burns are being considered. There is a great deal of difference between the injection of tannic acid directly into the subcutaneous tissues of animals and the application of tannic acid to a raw surface in a man when that raw surface is caused by a burn. These conditions are not comparable. It might be justifiable to compare observations in man with the results of experiments by other observers, mentioned by Wells, Humphrey and Coll, in which animals were burned, and after treatment with tannic acid jelly liver necrosis appeared. In his original paper E. C. Davidson pointed out that when tannic acid is applied to a burned surface in dilute solution, further penetration into the more deeply lying protoplasm is prevented by its precipitant action on the superficial body fluids and cells; the true astringent action is limited to the most superficial layers of tissue. On the other hand, as far as can be gathered the occurrence of liver necrosis in burns has been reported only after tannic acid treatment. Tannic acid and gentian violet were used as coagulants in the cases described by Wilson, Macgregor and Stewart, and it was after observing these cases that they described necrosis of the liver as the most striking feature of the pathology of burns. It would be interesting, and in point of fact it is necessary, to discover whether necrosis of the liver has been a feature of fatal cases of burning when tannic acid has not been used. What remains to be determined is whether hepatic necrosis occurs because of the use of tannic acid or in spite of it. In the meantime most clinicians will agree that when the accepted indications are present tannic acid should still be used.

¹ The British Journal of Surgery, Volume XXV, 1937-1938, page 826.

² The New England Journal of Medicine, April 16, 1942.

³ The Journal of Pathology and Bacteriology, Volume XLVIII, 1939, page 493.

Abstracts from Medical Literature.

GYNAECOLOGY.

The Treatment of Gonorrhoea in the Female with Sulphathiazole.

D. R. SMITH AND R. DRAMIN (*American Journal of Obstetrics and Gynecology*, February, 1942) advocate a routine treatment of gonorrhoea, divided into five stages: chemotherapy, local therapy, focal therapy, fever therapy and surgical therapy. Each, of course, is not necessarily used in every case, as chemotherapy effects a very large percentage of cures, and the authors are satisfied that a single five-day course of 30 grammes of sulphathiazole has been sufficient for cure in 94% of cases. Investigation by modern methods of culture of the gonococci is carried out to ensure that a cure has been obtained. They have found that fever therapy has been most effective in eradicating stubborn types of infection resistant to chemotherapy and the accepted local and focal measures.

Toxicity Studies on Stilbestrol.

A STUDY was undertaken by A. H. AARON (*The American Journal of Digestive Diseases*, November, 1941) to determine the toxic properties of stilbestrol. Thirty patients with chronic arthritis were treated with maximum doses of stilbestrol (one to three milligrammes daily for periods ranging from five to nine weeks, the patients receiving amounts varying from 55 to 189 milligrammes). The outstanding clinical observation was a marked improvement in general well-being in 80% of the group. Nausea occurred in 50%, but was controlled by reduction of dosage, and in no instance was it necessary to discontinue treatment because of this complaint. Post-menopausal bleeding was precipitated in twelve women, and when this occurred the drug was discontinued. Other symptoms elicited on inquiry were perspiration, headache, palpitation and urinary frequency. An analysis of the results of liver function tests (bilirubin excretion, hippuric acid excretion, icterus index, Van den Bergh, cholesterol, and cholesterol esters partition) both before and after treatment with stilbestrol revealed no evidence of liver damage. There was no significant change in the blood count, urine, blood urea level and blood glucose content after stilbestrol therapy.

Pregnancy and Hypertension.

BROWNE AND DODGE (*The British Journal of Obstetrics and Gynecology*, February, 1942) contribute a further article on the subject of pregnancy in the patient with chronic hypertension. Their conclusions are based on a series of 239 pregnancies in 222 patients. The standard of hypertension they adopt is a pressure of 130 millimetres of mercury (systolic) and 70 (diastolic). They state that if they had adopted the standard of 140 systolic and 90 diastolic, many of their most instructive and interesting cases of subsequent hypertension would have been excluded. Regarding the clinical features they were unable to confirm certain common beliefs. The bodily habitus of the patients was not constantly short and stocky. The authors' records did not support the impression that there was frequently a

family history of hypertension, though they admit that their research into this aspect of the subject was not complete, as relatives were not seen and examined. The average age of the 222 hypertensive patients was 31 years. Only two patients had pyelitis. The authors stress the point that most of the exacerbations were found after the thirtieth week of pregnancy. One statement is that "no woman with an initial blood pressure of 180 mm. of mercury or more (at the first visit) bore a live child". Pathological tests of renal efficiency and blood chemistry were practically useless. The most valuable investigation seemed to be of the blood urea. If the blood urea content was 30 milligrammes per one hundred cubic centimetres or over at the beginning of pregnancy the chance of a viable child was small. The immediate prognosis for the mother was good; but the fetal salvage rate was only 84%. The problem in treatment consists in making an initial decision about the advisability of terminating pregnancy of patients seen early with severe symptoms and signs. One should consider the termination of pregnancy in patients with an initial blood pressure of 180 millimetres of mercury, or a blood urea content of over 40 milligrammes per one hundred cubic centimetres, or with serious changes in the fundus oculi. In the vast majority of cases the pregnancy is allowed to proceed and a watching brief is held. The diet should be mainly vegetarian, and vitamins must be given freely. When the fetus reaches the stage of viability, about the end of the thirty-sixth week, pregnancy is terminated if the condition is getting worse. As the plasma prothrombin level in premature infants is low there is a considerable risk of cerebral hemorrhage and therefore the introduction of a rubber bougie is preferable to rupture of the membranes. Caesarean section is reserved for those few cases of elderly primiparae, in which the delivery of a live infant is especially important.

Cancer of the Cervix.

D. G. MORTON (*The Journal of the American Medical Association*, January 24, 1942) makes a plea for greater care in the early diagnosis of cervical cancer. The relatively small number of treated patients alive after five years is due to the fact that the majority of those affected seek treatment only after the disease is well established; the prognosis is then relatively hopeless. Prompt attention should be paid to the initial symptoms; measures to educate the public on this subject should be taken. Bleeding is the first symptom in the vast majority of cases; a thin, watery or foul discharge coming on initially or representing a change from a mucoid discharge is the first symptom in a smaller number of cases; in a few cases there are no significant symptoms. Patients often consider such abnormalities to be concomitants of the menopause, and medical practitioners have fallen into the same error. In every case of such hemorrhage or discharge, a vaginal examination is absolutely necessary, followed by further investigation if the cause is not at once clear. If no abnormality is found, the medical attendant should take the opportunity to apprise the patient of the symptoms whose occurrence would require immediate attention; but he need not mention the word

"cancer". The author considers that periodical examination should be advocated; women in the age group from about thirty-five to fifty years should be examined every six or twelve months. Medical practitioners should cultivate the ability to recognize cervical cancer—not always an easy task. The well-developed growth rarely causes difficulty, but small and hidden lesions may do so. In case of doubt a biopsy should be performed, but under conditions which will permit of immediate treatment if cancer is present, so that the dangers and drawbacks of biopsy may be avoided. A pathologist familiar with the varying microscopic appearances of tissue from the cervix is essential if a correct diagnosis is to be made. Schiller's test and the colposcope are of use in the diagnosis of early carcinomatous changes. The colposcope is an instrument to bring the surface of the cervix into greater magnification under intense illumination; the user should make himself familiar with normal and abnormal appearances. Schiller's test requires the instillation into the vagina of enough of the following solution to cover the cervix completely: one part of iodine, two parts of potassium iodide, 300 parts of water. After five minutes the solution is sponged out and the cervix is reinspected. Normal mucosa stains dark mahogany colour; eroded areas fail to stain; carcinomatous tissue appears dead white, and usually a distinct, well-defined border is seen between the normal and abnormal areas. The results of Schiller's test and the colposcopic findings are merely suggestive; if their limitations are recognized they can be of value, but they can never be considered diagnostic. The author concludes with the view that cancer is a special disease and that its management should be entrusted to those who are properly equipped to deal with it, or to special institutions; patients should have the benefit of the best facilities and knowledge available.

Vaginal Hysterectomy.

A. W. BLAIN (*Surgery, Gynecology and Obstetrics*, September, 1942) enters a plea for the wider use of vaginal hysterectomy. During a period of 30 years he and his associates have performed 1,564 vaginal hysterectomies. From the period January 1, 1925, to January 1, 1942, he himself has performed the operation 567 times with three deaths; his last 307 operations in four years have been without mortality. He quotes figures to show that the average surgeon using abdominal hysterectomy has a mortality of 5% or 6%, and sometimes 8% to 10%. He gives a long list of "advantages" of, and "indications" for, the operation. *Inter alia* the author observes that vaginal hysterectomy provides for the routine removal of the cervix which is too often not removed in abdominal hysterectomy.

Clinical Use of the Female Sex Hormones.

E. C. HAMLEN (*Surgery, Gynecology and Obstetrics*, February 16, 1942) discusses the use of the female sex hormones; these are of two types, oestrogenic substances (oestrogens) and progestational substances (progestin). Trial of oestrogen therapy has been justified in the following circumstances: (1) as supplemental or complemental

therapy in certain established instances of oestrogenic ovarian failure, in adolescence or sexual maturity; (ii) as palliative therapy only in certain subjective disturbances of the climacteric; (iii) in hypomastia, for cosmetic effects only; (iv) as antagonistic therapy in certain hyperfunctional states of other glands; (v) for specific pharmacological effects upon the vaginal epithelium, no endocrine disturbance being present. Progesterin (progesterone) has been tried as substitution or complementation therapy in *corpus luteum* deficiency during the progestational phase of the menstrual cycle or during pregnancy. The author concludes that oestrogenic hormones have a limited but established role in the treatment of certain climacteric manifestations, in gonorrhoeal vaginitis of childhood and in senile vaginitis. Complementary therapy with oestrogens and progesterone, in certain cases of intercurrent ovarian failure, may be followed by the return of normal ovarian function. In severe oestrogenic failure during adolescence or early maturity, substitution therapy gives only temporary results and does not relieve sterility. The occurrence of untoward responses to oestrogenic therapy is increasing since the introduction of cheap, orally active oestrogens; these responses are due to overdosage. The author urges care in avoiding over-treatment. Progesterone has not justified expectations as to its therapeutic role. Its best results have been achieved as a factor in cyclic steroid complementary therapy in oestrogenic bleeding. Its value in dysmenorrhoea and in repeated or threatened abortion is questioned. The author condemns the use of androgens in gynaecology; virilizing effects from their use do not always disappear when treatment is discontinued.

OBSTETRICS.

The Weight During Pregnancy.

EDWARD WATERS (*American Journal of Obstetrics and Gynecology*, May, 1942) writes on the study of the weight during pregnancy of 3,230 patients. In the first trimester there was an average gain of three pounds, in the second trimester a gain of a further eight pounds, and in the last trimester a gain of twelve pounds more. Altogether the average gain in weight of the mother was 23 pounds. The average gain of weight of the fetus was seven pounds. Patients who gain the average poundage during pregnancy may look forward to regaining their normal weight to within five pounds. The vast majority of all patients gaining an abnormal amount do not become toxemic; but the incidence of toxemia rises as gain of weight in excess of normal appears. In most instances fetal weight was not influenced by maternal changes in weight.

Vitamin E in the Prophylaxis of Abruptio Placentae.

EVAN SHUTE (*Surgery, Gynecology and Obstetrics*, October, 1942) states that *abruptio placentae* has been described as the premature separation of all or of a large portion of the normally implanted placenta. He holds that this condition can usually be recognized in its early stages by the appearance of small areas of uterine

tenderness, small uterine hemorrhages and evidences of incipient toxemia. The condition is characterized by a disturbance of the relationship between vitamin E and the oestrogens. The author presents in detail nine case reports to show first of all that the first clinical sign of placental detachment is a localized area of uterine tenderness, with or without slight bleeding or slight toxemia, and secondly that *abruptio placentae* can often be foreseen even earlier in pregnancy by a blood oestrogen assay. Such an assay in his opinion is a *sine qua non* for its early recognition. Moreover, if the signs are neglected the patient may go on to display the classical *abruptio placentae*. The early phenomena disappear promptly if enough vitamin E is administered at once. The vitamin E used must be a potent preparation. The dose usually rises as pregnancy proceeds and must always be calculated for the needs of the particular case in hand; no standard dose is possible. The use of vitamin E must be continued until delivery.

The Antenatal Use of Vitamin K.

NUMEROUS reports have been issued indicating that in infants whose mothers receive vitamin K a few hours before delivery, and in infants who receive the vitamin soon after birth, the blood prothrombin level is raised and the neonatal drop in prothrombin level is greatly reduced or entirely absent. J. Parks and L. K. Sweet (*American Journal of Obstetrics and Gynecology*, September, 1942) refer to two reports in which vitamin K was given to fairly large groups of women during labour; the authors of these reports recorded a reduction of neonatal hemorrhage among the infants of these mothers as compared with those whose mothers were not so treated. They have made a careful clinical analysis of gross hemorrhage occurring in the infants of mothers admitted to a municipal hospital. The mothers represented the lowest income group of a metropolitan area and it is regarded by the authors as reasonable to assume that dietary deficiencies and obstetric complications should be maximal in this group of patients. A single dose of five milligrammes of vitamin K was given by mouth at the time of their admission to hospital to the mothers of 1,151 infants; the infants of 1,594 mothers who received no vitamin K served as controls. The administration of vitamin K had no evident effect in reducing the incidence of neonatal hemorrhage. The vitamin raised the blood prothrombin levels of both the mothers and infants. If an elevated blood prothrombin level is a significant factor in preventing neonatal hemorrhage, the authors are unable to explain the results of their survey.

The Elderly Primigravida.

P. B. WAHRSINGER and J. I. KUSHNER (*American Journal of Obstetrics and Gynecology*, September, 1942) have made a study in a voluntary hospital with a closed staff (where the majority of patients are handled by general practitioners) in order to determine whether there is an increased risk in the labour of the "elderly primigravida". In this group is included the woman of thirty-five years of age and over who is pregnant for the first time. There were 111

such women among 10,333 delivered in four and a half years. The majority were in the 35-36 year age group. The pelvis was normal in 103 cases and contracted in eight. The common belief that the duration of labour among old primigravidae is usually longer than in the young patient is not borne out in this series; the average duration of labour was 18.9 hours. Labour terminated spontaneously in 49% of cases and the low forceps operation was employed in 28%. Mid-forceps operations were employed in only 9% of cases, all in the second stage; in three cases the cause was persistent occipito-posterior presentation, in three cases it was sudden fetal distress, and in four, lack of progress due to maternal inertia. Breech presentation occurred four times; three deliveries were spontaneous and in one case forceps had to be applied to the after-coming head. Caesarean section was performed in 13 cases, or 11.7%. The authors insist that the age of the patient was not the major indication for the performance of the operation; such potent contributing factors as pelvic deformity, progressive toxemia *et cetera* being present in the cases in which the operation was performed. The fetal mortality was twice as high among the children born to older patients as compared with a previous study of 10,000 cases. Three patients died, all after Caesarean section. No rules can be laid down for the conduct of labour of elderly primigravidae. Each case must be approached as an individual problem.

Placenta Praevia.

J. L. REYCHAFT and C. P. PLATE (*American Journal of Obstetrics and Gynecology*, September, 1942) state that *placenta praevia* is said by leading authorities to occur in from 1 in 200 cases to 1 in 2,000 cases. In a series presented by them, those occurring at the Cleveland Maternity Hospital in the ten-year period 1931 to 1940, the incidence was 160 in 20,498 cases, or 1 in 128 cases (0.8%). The high incidence is said to be due to the fact that the patients included most of those admitted to hospital from the outpatient department of the hospital. Of the 160 patients, 69 fell in the age group 20 to 29 years, and 71 in the age group 30 to 39 years; 52, or 33%, of them were primiparae. All the patients had signs of hemorrhage at the time of their admission to hospital and 67, or 42%, had pain; 21, or 13%, were suffering from profound shock; and 44, or 27.5%, required transfusions of blood before, during or immediately after delivery. Of all the patients 67% were delivered by Caesarean section. In the first few years the classical operation was usually performed, but since 1935 the transverse laparotomectomy has been used more and more. Braxton Hicks's version was used only once and in this case the child was not viable. The gross maternal morbidity was 37.5%. Of the 60 cases of maternal morbidity 24 consisted of fever of unknown origin, the fever was not severe and was of short duration; wound infection occurred in 13 cases and pelvic infection in 12. The uncorrected fetal mortality rate was 25%; if the non-viable fetuses and the premature deaths are excluded, the corrected fetal mortality was 8%. There were two maternal deaths.

Naval, Military and Air Force.

CLINICAL MEETING AT 119TH AUSTRALIAN GENERAL HOSPITAL.

A CLINICAL MEETING was held on August 23, 1942, at the 119th Australian General Hospital, Australia. The meeting took the form of a number of clinical demonstrations by members of the medical staff of the hospital.

Burns.

MAJOR H. K. PAVY showed a series of patients suffering from burns. The first, a man, aged twenty-one years, had been badly burnt on June 18, 1942, when a fuel oil tank exploded. First, second and third degree burns were received on the whole of the exposed portions of the body facing the fire. The burns involved both upper extremities from the backs of the fingers to the shoulder, the right side of the face and neck, and both lower extremities from the middle part of the thigh to the level of the sock on the right side of each. Immediate treatment consisted of the administration of a quarter of a grain of morphine, the application of tannic acid jelly, and the intravenous administration of one litre of dextrose in saline solution (5%) followed by one litre of plasma. Later a general anaesthetic was given, and the burns were dressed with triple dye and "Vaseline".

On June 18 the patient was transported by ambulance train to the 119th Australian General Hospital. On arrival his general condition was only fair; the dressings were satisfactory except for the face, which was oedematous and infected. The intravenous administration of plasma was started at 1400 hours, when his haemoglobin value was 102%. Four hours later his haemoglobin value had risen to 116%, so the administration of plasma was continued until four litres had been given. By the next day his general condition was much better and his haemoglobin value was 95%. Extreme thirst, acute discomfort and a rising temperature were present during the next few days. Saline baths and "Vaseline" gauze dressings were commenced on June 23. These measures relieved much of his discomfort, and with the softening of the coagulum, pus was able to escape and his temperature began to fall. Movements of all joints were commenced. During the next two weeks large areas of sloughing skin separated. Daily baths were continued until August 14. By this time all the burns were healed, with the exception of an area below the right shoulder approximately three inches in diameter, on to which skin was grafted, and the patient had a full range of movement in both arms, both legs and the neck.

Major Pavy's second patient was aged eighteen years; he had been badly burnt at the same time as the previous patient, and received similar but rather more severe burns of both upper and lower extremities, the face and the neck. The immediate treatment given was approximately the same, and he arrived at the 119th Australian General Hospital by ambulance train on June 18. His general condition was poor on admission to hospital and deteriorated rapidly. The haemoglobin value was 150%. Plasma infusion was commenced with difficulty, because the veins in his legs were collapsed and the fluid would not run. A vein in the ante-cubital fossa was exposed through the burnt area, and the infusion was commenced and maintained for two days. By this time seven litres of plasma had been given, and his haemoglobin value was 85%. The next few days were characterised by restlessness, extreme discomfort and thirst, and a temperature of 105° F. Treatment with daily saline baths, "Vaseline" gauze dressings and movements was commenced on June 22.

By July 28 the left arm was healed, the sloughs had all separated from the right arm and legs, the granulation tissue was healthy and a few epithelial islets were appearing. The patient's temperature still remained elevated, rising to 100° or 101° F. each evening. On August 3 the haemoglobin value had fallen to 40%, so 700 cubic centimetres of citrated blood were given. By August 18 his general condition was good, and he had full range of movement in all his joints except the fingers of the right hand. Although the granulations appeared healthy, culture revealed the presence of some *Bacillus coli communis* and other bacilli, and the growth of epithelium had slowed. The patient was sent to another hospital so that preparation for skin grafting could be carried out under better conditions.

The third patient shown by Major Pavy was aged twenty-one years. He had been burnt on July 8, when a tin of petrol exploded in a burning motor-car. The ignited petrol sprayed his body, and he had to roll in the dust to extinguish

the flames. The whole of his abdomen and chest above the belt line, both upper extremities, the neck, the face and a large area above the left knee were covered with first and second degree burns. There were small scattered areas of third degree burns. Before his admission to the 119th Australian General Hospital the whole of the burnt area had been treated with triple dye. This formed a thick, tough coagulum. His general condition was very good.

By July 13 he had become restless and uncomfortable; his temperature was 101° F., his pulse rate was 120 per minute, and he was complaining of tightness under the coagulum. Daily saline baths and "Vaseline" gauze treatment were commenced, and the coagulum was removed as soon as possible. On July 17 all the burns were clean and healthy, and by July 27 all areas with the exception of a few of the third degree burns were healed.

Major Pavy's fourth patient was aged nineteen years. He had been burnt on August 16, 1942, by a petrol explosion while he was repairing a motor car. His face and chest were covered with ignited petrol, which was extinguished by his mates. He had first and second degree burns on his face; first, second and small areas of third degree burns were present over the whole of his chest, his shoulders and the lower part of his neck. As a first-aid dressing, the burns had been covered with gauze soaked in acriflavine. On his admission to hospital these dressings were soaked off in a saline bath and "Vaseline" gauze was applied. By August 28 all the burnt areas were healed.

Major Pavy said that the treatment of burns was still a much discussed problem. Extensive burns were common, and the patients under discussion had been shown because of the recent interest in saline baths and the local difficulties due to climate, insects and lack of facilities. As soon as possible patients suffering from burns were put into baths of 1% saline solution; two full-length portable tin baths were used. Adequate supplies of cold sterile water were not available because of storage difficulties. Orderlies stood by to keep the flies away. While the patient was in the bath the old dressings were soaked off and the limbs were put through as full a range of movement as possible. This was very painful, and it was a heart-rending performance for both patient and surgeon. A scrubbed-up orderly then lifted the patient out of the bath on to a sterile sheet, which covered the whole bed. A sister, wearing sterile gloves and waited on by an assistant, then applied the gauze dressings over the whole burnt area. It had been found that mosquito net made the best dressings, the larger mesh permitting freer drainage. The net dressings were sterilized daily. Before the net was applied, the burns were dusted with sulphapyridine powder if any degree of infection was apparent. Major Pavy pointed out that it would be understood that with dust flying about, a strict aseptic régime was impossible; but the patients shown illustrated the results, which were presented for comment, criticism and advice.

Major Pavy suggested that in order to facilitate this form of treatment, if the patient could be sent to hospital quickly, his burns should be covered with sterile saline dressings or sterile "Vaseline" gauze as an emergency measure in the field, regimental aid post or field ambulance. If facilities existed enabling an anaesthetic to be given, in his experience "Pentothal Sodium" given intravenously was the best. Under anaesthesia a thorough removal of dead burnt skin could be carried out, and complete sterilization of the damaged area undertaken. Tanning was suitable for small burns on relatively flat, non-movable areas; but if an area was to be tanned, it must be done with every aseptic precaution on a surgically clean surface. In his experience practically every large tanned area became infected. These large areas also prevented early movement. Dye in particular formed a very dense, tough coagulum. Infection under such a coagulum acted in the same way as pus under pressure, and second-degree burns were converted into third-degree burns, with the resultant delays and discomforts. Major Pavy said that under the régime recommended the following points stood out: (i) Infection did not occur, or if it had already been established it cleared up quickly. (ii) Large dressings could be done with ease. (iii) The saline baths were of great comfort to the patients; they looked forward to them. (iv) Early movements were possible, so that contracture formation was prevented.

CAPTAIN W. G. HEASLER said that the pathologist had a part to play in the treatment of burns. From the haemoglobin estimation he could gauge exactly the amount of serum the patient required to restore his blood stream to normal; a 20% rise in the haemoglobin value meant that the patient required one pint of serum. The pathologist came in later also, when the wounds were healing and skin grafting was being contemplated. Skin grafting on a wound

area that was not sterile was apt to have rather disastrous results.

SURGEON LIEUTENANT-COMMANDER S. A. SEWELL said that he had had the opportunity of seeing all the patients shown, except the man with petrol burns, when they were first burnt; the burns were the first really severe burns that he had seen resulting from fuel fire. The men were extremely dirty and covered with a large amount of unburnt oil. Commander Sewell saw them only in the resuscitation stage, when they were suffering severely from shock and were obviously extremely ill. He handed them over to the hospital, where they were to receive further treatment. When he later saw the results of the early treatment they had received, he was inclined to think that the early treatment given was most unsatisfactory, because they had extremely thick and tough coagulum all over the burnt areas, early movement was not possible, and secondary infection might be expected. Subsequently, in all cases, immediately the initial shock had been treated, the patients were taken to the operating theatre; they were thoroughly cleansed in the usual way, and sterile dressings were applied. The result of this treatment was very rapid healing. All patients were discharged for duty within one month.

COLONEL E. H. BEARE asked Major Pavy what treatment he would like the regimental medical officer and the regimental aid post to carry out. There were two schools of thought regarding the treatment that should be given. Colonel Beare asked whether Major Pavy would prefer them not to use any of the coagulants, and if not, what they should use.

Major Pavy, in reply to Colonel Beare, said that he believed that the man in the regimental aid post had not the time to dress the wounds properly, and that he could use only what facilities and time he had. The best thing to do in such circumstances was to dress the burned areas with sterile gauze or lint soaked in sterile saline or acriflavine solution. Sterile "Vaseline" gauze might be used if available. In cases of burns of limited area away from flexures, on broad flat surfaces, Major Pavy still believed that tanning with tannic acid, silver nitrate or triple dye was good treatment. A sterile solution of soft soap was better than ethereal soap for cleansing the areas. In the case of extensive burns "Pentothal Sodium" anaesthesia was advisable during the cleansing process.

Partial Spontaneous Pneumothorax.

CAPTAIN T. R. NEVILLE showed a patient, aged thirty-two years. On July 1, 1942, the patient complained that he had had severe, stabbing, non-radiating precordial pain for three days. He had been suddenly awakened three nights previously by the pain, which had persisted; it was worse on movement and undoubtedly worse on coughing or deep breathing. For the three weeks prior to the appearance of these symptoms he had had a bad cold with considerable cough and sputum, not blood stained at any time. He stated that he had had no relevant previous sickness. He had done a considerable amount of physical culture and had done deep breathing exercises all his life.

On examination, the patient did not look ill. His general physique was fair, his pulse rate was normal and he was afebrile. No cardiac enlargement was detected and the heart sounds were normal. An area of pleuro-pericardial friction was audible about the apex. The lung expansion was the same on both sides; the note was resonant. A friction rub was present in the left axilla anteriorly. The breath sounds were diminished over the whole of the left lung. An X-ray examination of the chest on July 4 revealed that the heart was normal and the lung fields were clear. The patient was discharged to his unit, quite fit, on July 22.

On July 29 he was readmitted to hospital; he gave a similar story. This time he had had a slight cold for four days. On the morning prior to his admission he wakened and immediately noticed a pain similar in type and location to that described in his previous attack. It had persisted, and was still present when he was admitted to hospital. He did not look ill; he was not distressed, his pulse rate was normal and he was afebrile. The apex beat was not palpable, and the area of cardiac dullness was difficult to determine; the cardiac sounds were muffled to the left of the sternum, but well heard to the right of the sternum. There was a slight lag in the expansion of the left lung and the left side of the chest was hyperresonant. The breath sounds were greatly diminished over the whole of the left lung. Fremitus and resonance were unchanged. A friction rub was heard in the fifth left intercostal space in the mammary line. The trachea was centrally placed.

A provisional diagnosis of pneumothorax was made. A radiological and fluoroscopic examination was made on July 29. An adhesion to the left half of the diaphragm was present. A partial left pneumothorax with partial collapse of the lower portions of both lobes of the left lung was seen; no obvious pulmonary abnormality was detected. The heart appeared normal, and there was a slight shift of the mediastinum to the right. A further radiological examination was made on August 10. The pneumothorax was practically absorbed. There was still some collapse at the left apex and the left costophrenic angle, where an obvious adhesion was present. There was no evidence of tuberculosis. A third X-ray examination on August 20 revealed that the pneumothorax had almost completely disappeared. There was evidence of an adhesion to the left half of the diaphragm anteriorly. Examination of the sputum on several occasions failed to reveal acid-fast bacilli.

The course of the disorder was uneventful. The pain lasted intermittently for about four days after the patient's admission to hospital, and it returned for some hours on August 6. At the time of the meeting he felt and looked well, and his lungs were normal.

Captain Neville said that the most interesting features of the case were (i) the fact that the diagnosis was made before any radiological examination had been carried out, (ii) the aetiology and (iii) the prognosis. It would have been noted that the clinical signs were not completely typical of the condition. Captain Neville instanced the facts that the heart sounds were muffled to the left of the sternum, when no obvious degree of mediastinal shift could be detected, that the trachea was centrally placed, and that there was no change in fremitus or resonance. He thought that they were explained by the X-ray findings. There was some degree of mediastinal shift, and moreover, a portion of deflated lung appeared to be held in front of the heart. Again, the pneumothorax was of no great extent.

Captain Neville then discussed the possible aetiology of the condition. He said that on the first occasion a diaphragmatic pleurisy might have been present, which was not revealed by the X-ray examination. The adhesion was formed then. On the second occasion, some portion of this adhesion might have been torn from its attachment to the lungs and thus started the pneumothorax. A second possibility, and one which he considered the more likely, was that the condition on the first occasion was also a partial pneumothorax, which had disappeared by the time the X-ray picture was taken. The cause could have been the rupture of an emphysematous bulla. It had to be remembered that at that time the patient had a very severe cough, and this was the precipitating factor. Once again, when he developed a cough, it recurred. If that theory was correct, then the adhesion was but a "red herring". In the third place, Captain Neville thought that they had to consider, only to reject, the rupture of a subpleural tuberculous cavity into the pleural cavity. Such a happening was not so common as was generally thought. In the case under discussion, according to the results of X-ray and sputum examination, there was no evidence of such a possibility. Captain Neville said that the prognosis necessarily depended upon the aetiology. He considered that, as there seemed to be no gross abnormality underlying the condition, the prognosis was moderately good, though recurrence could not be excluded.

LIEUTENANT-COLONEL D. THOMAS said that he believed that there was no real doubt as to the diagnosis. He could not think that at any time was there a sufficient pressure for the pneumothorax cavity to produce any disastrous tearing of the pleural adhesion. Little was known about the aetiology of the condition. He remembered that in a recent review it was stated that at least 60% of these cases were not of tuberculous origin. It was most unlikely that the present one was of tuberculous origin. Non-tuberculous spontaneous pneumothorax was apt to recur, and with subsequent recurrence there was less mediastinal disturbance than with the initial occurrence. It was not possible to make a prognosis. Colonel Thomas thought it likely that the patient would have further attacks, but he had no idea as to when the next would occur.

Captain Neville asked what might be the disposal of such a patient.

LIEUTENANT-COLONEL J. H. HALLIDAY thought that the question of disposal should be the subject for a medical board. He felt that the man might carry on indefinitely. However, in view of the possibility of repeated attacks, Colonel Halliday thought that he should be removed temporarily from a field unit and given some other job, where he could be kept under review and not exposed to possible isolation in field service.

Gunshot Wound of the Right Thigh, Scrotum and Left Thigh.

LIEUTENANT-COLONEL C. A. M. RENOU showed a patient, aged twenty-four years, who had been admitted to hospital on July 19. There was a tangential wound of the upper anterior portion of the right thigh, involving skin and subcutaneous tissue only. The missile had passed through the scrotum from right to left, extensively lacerating the scrotal and penile skin and subcutaneous tissues. Both testicles were lying exposed in soft tissue hematomata; and the spermatic cords were intact. The bulb of the urethra was intact. A 12E rubber catheter was easily passed. The missile had passed through the left thigh from the inner side of the groin. The wound of exit was small and was below the greater trochanter. The bullet had passed between the femoral artery and the femur without damaging either structure.

Operation was undertaken four hours after the patient's admission to hospital. The right thigh was treated first; the skin edges and all damaged subcutaneous tissues were excised *en bloc*, and "Vaseline" and "Vaseline" gauze dressings were applied. The skin of the penis was loosely sutured with alkylworm gut; no excision was carried out. The scrotum was next dealt with; *débridement* of the blood-infiltrated soft tissues was carried out, and the testes were replaced after the hemorrhaging corpus cavernosus of the bulb had been sutured. Skin excision was minimal, and "Vaseline" was applied to the damaged tissues. Free drainage was established with no suturing. With regard to the left thigh, the skin edges were widely excised. The fascial tears were widely opened and excised. A foreign body was removed from the outer side of the thigh; it was lying loose in greatly "mushed up" muscle planes. The damaged muscle was widely removed and the track was impregnated with "Vaseline". No packing was used, and a "Vaseline" gauze dressing was applied to the wounds. An indwelling urethral catheter was introduced.

After the operation sulphapyridine was administered in the following dosage: four tablets were given every two hours for two doses, two tablets were given every four hours for five days, and two tablets were given three times a day for one day. In all, 37 grammes of "M & B 693" were given.

The wounds were untouched for seven days, and the catheter was removed after seven days.

Colonel Renou said that the patient had been presented to show what happened when a perforating gunshot wound of the thigh was correctly treated. The wounds of entrance and exit were small, and those of the deep fascia were smaller; but when the deep fascia was widely incised and its edges were removed, all tension was seen to disappear in the limb with the evacuation of the blood clot and removal of the retained part of the missile and the extensively damaged muscle. It was interesting to see how damaged and "mushed up" the muscle was when the skin wounds of entry and exit were so small. This muscle damage always occurred, and unless drainage was adequate subsequent trouble ensued. Drainage could be established only by widely opening the whole wound and leaving it open without tension. "Vaseline" treatment of the track promoted drainage, and no plugging should ever be used. Colonel Renou said that he had on many occasions seen men with similar gunshot wounds four or five days after operation, looking very ill, with hectic temperatures and with wounds plugged. When the plugs were removed, a gush of pus under tension followed. It was about a month since the patient had been wounded; the wound was practically healed, and there had been no undue rise in temperature. His general condition had remained good throughout, and he had given no cause for worry at any stage.

Colonel Renou further drew attention to a comparison of the thigh wound with that of the scrotum. In the scrotum a less thorough excision was made, in an attempt to retain intact a more vital part. Suppuration was obviously free; however, the patient would retain his testicles, and his urethra had remained intact without stricture formation. It had been necessary to prolong the time spent in convalescence, in order to retain the structure and the function of the parts concerned.

CAPTAIN E. B. DOCKER asked whether there was any objection to the use of rubber drains in that type of wound.

CAPTAIN F. HIDE (United States Army) thought the result obtained excellent; the tissues had been given as much chance as possible to heal under optimal conditions. Captain Hide asked what was the present view regarding the local use of sulphonamide drugs in such wounds.

Colonel Renou, in reply to Captain Docker, said that if the excision was wide a rubber drain would not be necessary.

Gauze plugging should not be confused with rubber drains. Gauze plugging was criminal in war wounds of that type. In reply to Captain Hide, Colonel Renou said that the use of sulphonamide drugs was the one point which had been under constant discussion in the Middle East. After an analysis had been made of a series of cases treated with "M & B 125" powder, "M & B 693" powder, "M & B 693" powder in "Vaseline", or "Vaseline" alone, the opinion was formed that the results did not differ materially one from the other. The factor of prime importance was adequate drainage with relief of all tension. Colonel Renou believed that the local use of "Vaseline" was invaluable.

(To be continued.)

APPOINTMENTS.

THE undermentioned appointments have been promulgated in the *Commonwealth of Australia Gazette*, Number 309, of November 26, 1942.

CITIZEN NAVAL FORCES OF THE COMMONWEALTH. *Royal Australian Naval Reserve.*

Appointments.—Walter Selwyn Georgeon, Kenneth Newton Speed and Donald Kerr Grant are appointed Surgeon Lieutenants, dated 22nd September, 1942, 3rd October, 1942, and 15th October, 1942, respectively; Lindsay Vaughan Carter and Douglas Lockhart Barnes Fearon are appointed Surgeon Lieutenants, dated 5th October, 1942.

CASUALTIES.

ACCORDING to the casualty list received on November 27, 1942, Major R. N. Howard, A.A.M.C., of Toorak, Victoria, is reported to have been wounded in action overseas.

According to the casualty list received on December 1, 1942, Captain D. J. Brennan, A.A.M.C., of Sydney, New South Wales, who was previously reported missing, is now reported to be a prisoner of war.

Correspondence.

THE TREATMENT OF BURNS.

SIR: Recent articles on the wet treatment of burns mention normal saline as the solution to be used. I regard this as a very crude method. The English physiologist, Sydney Ringer, first showed that a heart perfused in normal saline stopped beating and needed other metallic ions to restore motion.

Locke's solution containing sodium, potassium, calcium, and glucose enabled the mammalian heart to keep beating.

I think therefore that in burns Locke's solution would be a vast improvement on normal saline. For delicate work blood serum is a great improvement on both of them, especially with a little sulphanilamide added.

Yours, etc.,

F. W. SIMPSON.

Mercantile Mutual Building,
179, St. George's Terrace,

Perth,

November 20, 1942.

ESOPHAGEAL FISTULA IN THE RIGHT LOIN.

SIR: About fifteen years ago I had a similar case as described by Dr. Denning (*THE MEDICAL JOURNAL OF AUSTRALIA*, September 26, 1942). As it was impossible to operate with success I tried to close the fistula by means of chemical irritation. I used the so-called Frank solution (zinc sulphate, 6-0; copper sulphate, 6-0; redistilled distilled water ad 100-0).

My case had only one opening at the loin, and after putting the patient on the operating table we raised the pelvis. A long, blunt and large and wide needle was inserted into the opening at the loin and the solution injected with gentle pressure. After a short time the patient complained

of a tickling sensation in the oesophageal opening, which forced him to cough up some phlegm with bluish saliva. Then we closed the lower opening with a pressure bandage. The following day the discharge was increased on account of the chemical irritation. On the fifth day after the first injection we gave another one, and at the same time when the tickling at the opposite opening started the patient got some colloidal mixture (which corresponds to the "Amphojel" of Wyeth's) in order to protect the epithelium of the oesophagus. Altogether the patient received about ten doses which gradually became more and more difficult to inject. After about six weeks the discharge of the lower opening stopped and the patient was free from any complaints.

Yours, etc.,

H. KAUFMAN.

207, King William Road,
Hyde Park,
Adelaide,
South Australia.
October 23, 1942.

"MUST THERE BE A REVOLUTION IN MEDICAL PRACTICE?"

SIR: Dr. Stanley Boyd in his letter dated October 16 cites what he describes as "two considerations fundamental to the problem": (I) The essential inequity of the present method of private practice. (II) The march of scientific progress.

Let us consider equity (or inequity in his letter) and scientific progress.

Is there anything more equitable than that we should each pay for the services that we render to each other? It is reliably reported of a retriever dog that goes to a café every morning to get food for his invalid master. The waitress puts the food in a paper bag, and, taking the coin from the dog's mouth, replaces the coin with the food. Efforts to "trick" the dog have failed. There is no ceremony or fuss, the waitress scarcely interrupting her duties to attend to the dog!

As for practical scientific progress, has anything more British been established both as regards science and progress as far as medicine is concerned, than the Burroughs Wellcome Institute in London, or the David G. Bull Laboratory in Melbourne? And many other instances could be cited.

The various faculties, namely, medicine, law, arts *et cetera*, are quite capable of administering their own professional and business affairs.

Where our serious trouble lies is in the lack of practical cooperation with and cohesion between the related sciences. At the University, the various schools of arts, science, veterinary, law, medicine and agriculture *et cetera* may be more or less in touch with one another; but what becomes of this relationship when we leave our Alma Mater?

Yours, etc.,

J. L. WHITWORTH.

Kalorama,
Victoria,
Undated.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Practitioners Act, 1938-1939*, of New South Wales, as duly qualified medical practitioners:

Chrichtlow, Nathaniel, M.B., Ch.B., 1913 (Univ. Glasgow),
co. British Solomon Islands Protectorate Government, 17, Castlereagh Street, Sydney.
Faragher, Erskine Christian, M.R.C.S. (England),
L.R.C.P. (London), 1920, Arian Park, New South Wales.
Phillips, Helen Mary, M.B., B.S., 1942 (Univ. Sydney),
Children's Hospital, Melbourne.
Phillips, Garth Jowett Blunden, M.B., B.S., 1942 (Univ. Sydney), Sydney Hospital, Sydney.
Pigott, Francis Paton, M.B., B.S., 1942 (Univ. Sydney),
Royal Prince Alfred Hospital, Camperdown.
Pittar, Desmond John, M.B., B.S., 1942 (Univ. Sydney),
District Hospital, Wallsend.

Pope, David Carington, M.B., B.S., 1942 (Univ. Sydney),
Royal Prince Alfred Hospital, Camperdown.
Powys, Norman Skelton, M.B., B.S., 1942 (Univ. Sydney),
Saint George District Hospital, Kogarah.
Rae, John Morell, M.B., B.S., 1942 (Univ. Sydney), Sydney
Hospital, Sydney.
Robertis, Alan Peter, M.B., B.S., 1942 (Univ. Sydney),
Newcastle Hospital, Newcastle.
Robey, Lancelot Turbet, M.B., B.S., 1942 (Univ. Sydney),
Western Suburbs Hospital, Croydon.
Robinson, Raymond George Rokeby, M.B., B.S., 1942
(Univ. Sydney), Royal North Shore Hospital, Saint
Leonards.
Rodriguez, Laurence Francis, M.B., B.S., 1942 (Univ.
Sydney), Sydney Hospital, Sydney.
Roskin, Nathaniel Neville, M.B., B.S., 1942 (Univ.
Sydney), Royal Prince Alfred Hospital, Camperdown.
Ross, Heather June Sylvia, M.B., B.S., 1942 (Univ.
Sydney), District Hospital, Lithgow.
Rowe, Charles, M.B., B.S., 1942 (Univ. Sydney),
Lewisham Hospital, Lewisham.
Segal, Harry, M.B., B.S., 1942 (Univ. Sydney), Sydney
Hospital, Sydney.
Simpson, Ian Gordon, M.B., B.S., 1942 (Univ. Sydney),
Sydney Hospital, Sydney.
Storey, David Maxwell, M.B., B.S., 1942 (Univ. Sydney),
Royal Prince Alfred Hospital, Camperdown.
Sutton, David Harvey, M.B., B.S., 1942 (Univ. Sydney),
Royal Prince Alfred Hospital, Camperdown.
Swain, John Phillip, M.B., B.S., 1942 (Univ. Sydney),
Western Suburbs Hospital, Croydon.
Tansey, Laurence Edward, M.B., B.S., 1942 (Univ.
Sydney), Saint Vincent's Hospital, Darlinghurst.
Thomas, David Lloyd, M.B., B.S., 1942 (Univ. Sydney),
Royal North Shore Hospital, Saint Leonards.
Turk, Harvey Coleman, M.B., B.S., 1942 (Univ. Sydney),
Sydney Hospital, Sydney.
Tyrer, John William Howard, M.B., B.S., 1942 (Univ.
Sydney), Royal Prince Alfred Hospital, Camperdown.
Vickers, Thomas Harold, M.B., 1942 (Univ. Sydney),
Sydney Hospital, Sydney.
Waddy, John Archibald, M.B., 1942 (Univ. Sydney),
Royal Hobart Hospital, Hobart, Tasmania.
Wallman, Peter Halcomb, M.B., B.S., 1942 (Univ.
Sydney), Royal North Shore Hospital, Saint
Leonards.
Walton, Frank Westlake, M.B., B.S., 1942 (Univ. Sydney),
Royal Hobart Hospital, Hobart, Tasmania.
Watson, Charles Rolleston, M.B., B.S., 1942 (Univ.
Sydney), Lewisham Hospital, Lewisham.
Webb, Pauline Hopwood, M.B., B.S., 1942 (Univ. Sydney),
Sydney Hospital, Sydney.
Wiles, Ronald Booth, M.B., B.S., 1942 (Univ. Sydney),
Royal Prince Alfred Hospital, Camperdown.
Yuille, Alexander Loddon, M.B., B.S., 1942 (Univ. Sydney),
Royal Prince Alfred Hospital, Camperdown.
Yuille, Archibald Binnie, M.B., B.S., 1942 (Univ. Sydney),
Royal North Shore Hospital, Saint Leonards.
Evans, Margaret Mabel, M.B., B.S., 1932 (Univ. Adelaide),
D.R.C.O.G., London, 1942, 7, Turaga Street,
Turramurra.

The following additional qualifications have been registered:

Cooper, Alfred Leonard (M.B., Ch.M., 1925, Univ. Sydney), D.P.M., 1942 (Univ. Sydney), Mental Hospital, Morisset.
Mayes, Bruce Toomba, R.A.A.F. (M.B., B.S., 1927, Univ. Sydney), F.R.C.S., 1931, Edinburgh, F.R.A.C.S., 1933, M.R.C.O.G., 1935, London.
Roberts, Frederick Gregory, Sydney (M.B., Ch.M., 1926, Univ. Sydney), F.R.A.C.S. (Ophthalmology), D.O. (Oxon), D.O.M.S. (England).
Van Someren, Bertram, Department of Public Health, Sydney (M.B., 1915, Ch.M., 1916, Univ. Sydney), D.P.H., 1939, Univ. Sydney.

QUEENSLAND.

THE undermentioned have been registered pursuant to the provisions of the *Medical Acts, 1939-1940*, of Queensland, as duly qualified medical practitioners:

Bennett, Noela Wynifred, M.B., B.S., 1942 (Univ. Sydney),
General Hospital, Brisbane.
Best, Judith Kane, M.B., B.S., 1939 (Univ. Sydney),
Wirringulla, Guy Street, Warwick.

Birkbeck, Knid Mary, M.B., B.S., 1942 (Univ. Sydney), General Hospital, Brisbane.
 Gray, Helen Patricia, M.B., B.S., 1942 (Univ. Sydney), General Hospital, Brisbane.
 Lewis, Braham Ralph, M.B., B.S., 1942 (Univ. Melbourne), General Hospital, Brisbane.
 Millikan, Milton Russell, M.B., B.S., 1942 (Univ. Melbourne), General Hospital, Brisbane.
 Douglas, George Alexander Scouller, M.B., B.S., 1942 (Univ. Melbourne), General Hospital, Brisbane.
 McKenzie, Mavis Hinemoa, M.B., B.S., 1941 (Univ. Sydney), General Hospital, Brisbane.
 Letham, Donald David, M.B., B.S., 1942 (Univ. Melbourne), General Hospital, Brisbane.

Nominations and Elections.

THE undermentioned have been elected as members of the New South Wales Branch of the British Medical Association:
 Jones, Allan Hackett, M.B., B.S., 1942 (Univ. Sydney), Prince Henry Hospital, Little Bay.
 Keston, Frank Keston Cyrus, M.B., B.S., 1941 (Univ. Sydney), Teralba.
 Ross, Heather June Sylvia, M.B., B.S., 1942 (Univ. Sydney), District Hospital, Lithgow.
 Walton, Frank Westlake, M.B., B.S., 1942 (Univ. Sydney), 37, Morton Street, Wollstonecraft.
 Wilson, Humbert, recommended and approved for registration in terms of Section 17 (2) of the *Medical Practitioners Act, 1933-1939* (February 4, 1942), Waterfall Sanatorium, Waterfall.
 Moore, Howard Stewart, M.B., B.S., 1942 (Univ. Sydney), Sydney Hospital, Sydney.

Obituary.

NEIL MCCOLL.

We regret to announce the death of Dr. Neil McColl, which occurred on November 19, 1942, at Maffra, Victoria.

WILLIAM GEORGE CUSCADEN, JUNIOR.

We regret to announce the death of Dr. William George Cuscaden, junior, which occurred on November 26, 1942, at Yenna, Lower Plenty, Victoria.

JOHN SUMNER MARTIN.

We regret to announce the death of Dr. John Sumner Martin, which occurred on November 30, 1942, at Footscray, Victoria.

JOHN CLEVELAND BEST.

We regret to announce the death of Dr. John Cleveland Best, which occurred on November 30, 1942, at Rose Bay, New South Wales.

FREDERICK HENRY COX.

We regret to announce the death of Dr. Frederick Henry Cox, which occurred on December 5, 1942, at Helensburgh, New South Wales.

Medical Appointments.

Dr. George Murch Haydon has been appointed Public Vaccinator in the Department of Public Health, Victoria.

Captain Frederic Boyd Turner has been appointed an Officer of Health at Cook and in areas adjacent, under the provisions of the *Health Act, 1935-1941*, of South Australia.

Dr. Neill Horace Munday has been appointed to be Temporary Honorary Assistant Surgeon at the Royal Adelaide Hospital.

Dr. John Fisher Williams, pursuant to the provisions of the *Public Service Act, 1928*, of Victoria, has been appointed Medical Officer, Classes "C" and "B", Professional Division, Mental Hygiene Branch, Department of Mental Hygiene.

Dr. Charles Patrick Gordon has been appointed Government Medical Officer at Singleton.

Books Received.

"The Personal Factor in Accidents", Emergency Report Number 3 of the Medical Research Council Industrial Health Research Board; 1942. London: His Majesty's Stationery Office. 10" x 6", pp. 19. Price: 4d. net.

Diary for the Month.

DEC. 15.—New South Wales Branch, B.M.A.: Medical Politics Committee.
 DEC. 18.—Queensland Branch, B.M.A.: Council.
 DEC. 25.—Tasmanian Branch, B.M.A.: Council.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmalm United Friendly Societies' Dispensary; Leichhardt and Peteraham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phoenix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 235, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 173, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia.

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